

Author	Year	HERO ID	Redirect from	Exclude?	Standardized justification
Goldey et al.	1995	47251		no	N/A
Goldey and Crofton	1998	51027		no	N/A
Lilienthal and Winneke	1991	66506		no	N/A
Widholm et al.	2001	103780		no	N/A
Gerstenberger and Tripoli	2001	116863		no	N/A
Lasky et al.	2002	116876		no	N/A
Steinberg et al.	2007	116896		no	N/A
Kodavanti et al.	1998	130226		no	N/A
Bowers et al.	2004	150620		no	N/A

Endpoints Evaluated	Endpoint Category	Test compound	PCB Mixture or Congener?
motor development auditory startle response, auditory thresholds	Motor function Sensory function	Aroclor 1254	Mixture
acoustic startle response locomotor activity reflex modification audiometry	Emotional state Motor function Sensory function	Aroclor 1254	Mixture
visual discrimination learning (lashley jumping stand and retention) active avoidance learning (shuttle box)	Cognitive-behavioral tests Emotional state	Clophen A30	Mixture
spatial discrimination reversal learning (2 lever operant testing chambers)	Cognitive-behavioral tests	Aroclor 1254	Mixture
surface righting, negative geotaxis, reflex suspension	Motor function	Aroclor 1016	Mixture
cochlear function (distortion product otoacoustic emissions), auditory evoked brain stem responses	Sensory function	Aroclor 1254	Mixture
locomotor activity (ambulation between chambers) female sexual behavior (paced mating), vocalizations	Motor function Social behavior	Aroclor 1221	Mixture
regional brain weights locomotor activity neurotransmitter levels (DA, NE, 5-HT)	Brain-histological, structural, morphological Motor function Neurotransmitter levels	Aroclor 1254	Mixture
grip strength, righting reflex, negative geotaxis	Motor function	Aroclor 1254	Mixture

<b>t<sub>1/2</sub> (half-life of test compound in days)</b>	<b>Species</b>	<b>Strain</b>	<b>Primary exposure route (oral, inhalation, injection, dermal)</b>
	Rat	Long-Evans	Oral-gavage
	Rat	Long-Evans	Oral-gavage
	Rat	Wistar	Oral-diet
	Rat	Long-Evans	Oral-gavage
	Rat	Long-Evans	Injection-ip
	rat	Long-Evans	Oral-gavage
	rat	Sprague-Dawley	Injection-ip
	Rat	Long-Evans	Oral-gavage
	Rat	Sprague-Dawley	Oral-cookie

Notes (general)
MOA, rescue effects with T4
all behavioral tasks were only performed in male pups. Examined max of 2 individuals per litter. Behaviors were monitored at PND 120 and PND 180. Reported PCB tissue levels in liver and brain.
provides AR1254 Lot #
MOA, rescued effects with T4
auditory function assessed at 18 months of age
dosing was only 5 days/wk for 4 wks
doses were delivered using teddy graham cookies



Meerts et al.	2004	150660		no	N/A
Lilienthal et al.	1990	198619	2173281	no	N/A
Levin et al.	1988	198621		no	N/A
Linder et al.	1974	198624		no	N/A
Becker et al.	1979	198634		No	N/A
Arnold et al.	1993	198641	2152475	No	N/A
Pantaleoni et al.	1988	198866	199738, 2206865	no	N/A
Casey et al.	1999	199578		no	N/A
Arnold et al.	1997	199648	2199097	no	N/A
Crofton et al.	2000	199653		no	N/A
Arnold et al.	1999	199657		no	N/A

brain weight	Brain-histological, structural, morphological	Aroclor 1254	Mixture
operant conditioning active avoidance learning, open field testing	Cognitive-behavioral tests Emotional state	Clophen A30	Mixture
delayed spatial alteration (spatial learning and memory)	Cognitive-behavioral tests	Aroclor 1016 Aroclor 1248	Mixture
brain weight and histopathology	Brain-histological, structural, morphological	Aroclor 1254 Aroclor 1260	Mixture
lethargy	Neurological symptoms	Aroclor 1242	Mixture
demeanor	Emotional state	Aroclor 1254	Mixture
active avoidance, open field activity reflex development (surface righting, cliff avoidance, negative geotaxis), swimming	Emotional state Motor function	Fenclo 42	Mixture
open field behavior	Emotional state	Aroclor 1242	Mixture
brain weight; brain and nerve histopathology	Brain-histological, structural, morphological	Aroclor 1254	Mixture
auditory thresholds via reflex modification audiometry (PND 92-110), histological examination of cochlea	Sensory function	Aroclor 1254	Mixture
brain weight	Brain-histological, structural, morphological	Breast milk mixture: PCBs 52, 66, 74, 105, 118, 138, 153, 156, 157, 180, 183, 187, 189, 194, 203	Mixture

	Rat	Wistar	Oral-gavage
	Rat	Wistar	Oral-diet
	Rhesus monkey	Macaca Mulatta	Oral-diet
	Rat	Sherman	Oral-diet
	Rhesus monkey	Macaca Mulatta	Oral-diet
	Rhesus monkey	Macaca Mulatta	Oral-capsule
	Rat	Fischer 344	Injection-ip Oral-gavage
	Rat	Sprague-Dawley	Inhalation Oral-diet
	Rhesus monkey	Macaca Mulatta	Oral-capsule
	Rat	Long-Evans	Oral-gavage
	Cynomolgus monkey Rhesus monkey	Macaca Fascicularis Macaca Mulatta	Oral-syringe

<p>Also evaluated neurotransmitter levels; these results are reported in HERO #626549</p> <p>Also evaluated mating frequency, but not enough information was provided to consider this an assay of social behavior</p>
<p>all behavioral tasks were only performed in male pups. Examined max of 2 individuals per litter? Behaviors were monitored at both PND 22 and PND 120. Contains PCB tissue levels in liver and brain.</p>
<p>examined &gt;1 AR mixture. Includes subsequent births from the same dam (multi-generational)</p>
<p>performed LD50 experiments with both diet and IV injections. Then performed 2 generation reproductive assays. No neurological data presented. Brain weights were measured, but not reported.</p>
<p>Primarily female repro study but there is some analysis of frequency of occurrence of outcomes</p>
<p>used whole body inhalation. Compares inhalation and dietary exposure, ADME, also examines TH levels.</p>
<p>Contains ADME data for infants and moms</p>
<p>MOA ototoxicity</p>

Bushnell et al.	2002	199676		no	N/A
Overmann et al.	1987	199680		no	N/A
Rice et al.	1998	199689	2195916	no	N/A
Crofton et al.	2000	199692		no	N/A
Kaya et al.	2002	199715		no	N/A
Schantz et al.	1989	199761		no	N/A

<p>acquisition of visual discrimination, performance of a visual signal detection task</p> <p>activity level, arousal, handling reactivity, excitability, motor activity, habituation of motor activity</p> <p>ataxia, gait abnormalities, tremors, landing foot splay, grip strength, aerial righting ability</p> <p>responses to sensory stimuli: auditory, somatosensory, and nociception; pupil constriction</p>	<p>Cognitive-behavioral tests</p> <p>Emotional state</p> <p>Motor function</p> <p>Sensory function</p>	Aroclor 1254	Mixture
<p>electroshock seizure phases</p> <p>duration, brain weight</p> <p>negative geotaxis, air righting, forepaw suspension</p> <p>auditory startle</p>	<p>Brain-histological, structural, morphological</p> <p>Motor function</p> <p>Sensory function</p>	Aroclor 1254	Mixture
<p>3 spatial discrimination reversal tasks, differential reinforcement of low rate (DRL) 30-s schedule</p> <p>initiation reversal tasks</p>	Cognitive-behavioral tests	Breast milk mixture: PCBs 52, 66, 74, 105, 118, 138, 153, 156, 157, 180, 183, 187, 189, 194, 203	Mixture
<p>acoustic startle response</p> <p>auditory thresholds</p>	<p>Emotional state</p> <p>Sensory function</p>	Aroclor 1254	Mixture
<p>brain weight</p> <p>conditioned place preference, sweet preference</p>	<p>Brain-histological, structural, morphological</p> <p>Emotional state</p>	Breast milk mixture: PCBs 28, 77, 101, 105, 118, 126, 138, 146, 153, 156, 169, 170, 180, 187	Mixture
<p>two choice discrimination reversal learning (spatial, color, and shape)</p>	Cognitive-behavioral tests	Aroclor 1016 Aroclor 1248	Mixture

	Rat	Long-Evans	Oral-gavage
	Rat	Wistar	Oral-diet
	Cynomolgus monkey	Macaca Fasicularis	Oral-syringe
	Rat	Long-Evans	Oral-gavage
	Rat	Long-Evans	Oral-diet
	Rhesus monkey	Macaca Mulatta	Oral-diet

sensory effects



Powers et al.	2009	199798		no	N/A
Rice et al.	1997	199799		no	N/A
Bowman et al.	1981	199846		no	N/A
Rice and Hayward	1997	199848		no	N/A
Rice and Hayward	1999	199869		no	N/A
Roegge et al.	2000	199872		no	N/A
Roegge et al.	2006	199873		no	N/A
Morse et al.	1996	201472		no	N/A
Rosin and Martin	1981	201490		no	N/A
Seegal et al.	1986	201511		no	N/A

brain-to-body wt. ratio auditory function assessed at PND 200 distortion product otoacoustic emissions (DPOAEs) and auditory brainstem responses (ABRs)	Brain-histological, structural, morphological Sensory function	Fox River PCB mixture	Mixture
multiple fixed interval (FI) fixed ratio, interresponse times	Cognitive-behavioral tests	Breast milk mixture: PCBs 52, 66, 74, 105, 118, 138, 153, 156, 157, 180, 183, 187, 189, 194, 203	Mixture
locomotor activity	Emotional state Motor function	Aroclor 1248	Mixture
nonspatial discrimination reversal problems, spatial delayed alternation task	Cognitive-behavioral tests	Breast milk mixture: PCBs 52, 66, 74, 105, 118, 138, 153, 156, 157, 180, 183, 187, 189, 194, 203	Mixture
relative reinforcement schedule and progressive ratio schedule	Cognitive-behavioral tests	Breast milk mixture: PCBs 52, 66, 74, 105, 118, 138, 153, 156, 157, 180, 183, 187, 189, 194, 203	Mixture
spatial learning and memory using the radial arm maze	Cognitive-behavioral tests	Aroclor 1254	Mixture
cerebellar histopathology	Brain-histological, structural, morphological	Aroclor 1254	Mixture
regional brain levels of dopamine (DA), 5- hydroxytryptamine (5-HT), and norepinephrine (NE)	Neurotransmitter levels	Aroclor 1254	Mixture
locomotor activity, rotarod, screen test seizure activity	Motor function Neurophysiology	Aroclor 1254	Mixture
serotonin (5-HT) and serotonin metabolite levels (5-HIAA) in various brain regions (frontal cortex, hippocampus, hypothalamus, and lateral olfactory bulb)	Neurotransmitter levels	Mixture: Aroclors 1254, 1260	Mixture

	Rat	Long-Evans	Oral-cookie
	Cynomolgus monkey	Macaca Fasicularis	Oral-syringe
	Rhesus monkey	Macaca Mulatta	Oral-diet
	Cynomolgus monkey	Macaca Fasicularis	Oral-syringe
	Cynomolgus monkey	Macaca Fasicularis	Oral-syringe
	Rat	Long-Evans	Oral-gavage
	Rat	Long-Evans	Oral-cookie
	Rat	Wistar	Oral-gavage
	Mouse	CD1	Oral-gavage
	rat	Wistar	Oral-gavage

includes brain/serum levels of PCBs-ADME
includes brain/serum levels of PCBs-ADME

Seegal et al.	1991	201512		no	N/A
Seegal et al.	1994	201513		no	N/A
Abrahamson and Allen	1973	201746		no	N/A
Allen and Abrahamson	1973	201750		no	N/A
Allen et al.	1974	201755		No	N/A
Aulerich et al.	1985	201773	2152680	no	N/A
Bowman and Heironimus	1981	201796	2201021	no	N/A

concentrations of dopamine and its metabolites in the caudate, putamen, substantia nigra, and hypothalamus	Neurotransmitter levels	Aroclor 1016 Aroclor 1260	Mixture
concentrations of dopamine in the caudate nucleus, putamen and substantia nigra	Neurotransmitter levels	Aroclor 1016 Aroclor 1260	Mixture
brain weight	Brain-histological, structural, morphological	Aroclor 1248	Mixture
brain weight	Brain-histological, structural, morphological	Aroclor 1248 Aroclor 1254 Aroclor 1262	Mixture
lethargy	Neurological symptoms	Aroclor 1248	Mixture
brain weight neurotransmitter levels in various brain regions	Brain-histological, structural, morphological Neurotransmitter levels	Aroclor 1254	Mixture
locomotor activity	Emotional state Motor function	Aroclor 1248	Mixture

	Pigtail monkey	Macaca Nemestrina	Oral-cookie
	Pigtail monkey	Macaca Nemestrina	Oral-cookie
	Rhesus monkey	Macaca Mulatta	Oral-gavage
	Rat	Sprague- Dawley	Oral-diet
	Rhesus monkey	Macaca Mulatta	Oral-gavage
	Mink	Mustela Vison	Oral-diet
	Rhesus monkey	Macaca Mulatta	Oral-diet

ADME- also includes brain measurements by congeners

This may be the same animals in 202763

dose administered needs some extrapolation

also evaluated reproductive, endocrine, hepatic, metabolic (body weight), endpoints

testing took place 44 months after exposure- I believe these are the same organisms studied in another Bowman report, but with the testing repeated at an older age.

Duplicate entry said "other information is reported in sister reports. Authors hypothesize that measured behavior 4 years after initial PCB exposure and after clearance of measurable PCB residues from mesenteric fat demonstrate that developmental changes are enduring and irreversible"



Bowman et al.	1978	201797		no	N/A
Bruckner et al.	1973	201809	2155498	no	N/A
Chu et al.	1980	202194		no	N/A
Freeman et al.	2000	202272		no	N/A
Hansen et al.	1975	202309		no	N/A
Hansen et al.	1976	202313	2165171	no	N/A
Hany et al.	1999	202314		no	N/A

WGTA discrimination tests and general procedure spatial reversals, color reversals, shape discrimination reversals, partial reinforcement, probability learning, progressive probability shift, object alternation learning, object alternation learning set locomotor activity test	Cognitive-behavioral tests Motor function	Aroclor 1248	Mixture
brain histopathology diminished exploratory behavior, unusual stance and gait, decreased response to pain stimuli chromodacryorrhea	Brain-histological, structural, morphological Neurological symptoms Neurotransmitter levels	Aroclor 1242	Mixture
brain histopathology	Brain-histological, structural, morphological	Aroclor 1254 Aroclor 1260	Mixture
histopathological analysis of brain tissues functional observational battery: open field functional observational battery: spontaneous locomotor behavior	Brain-histological, structural, morphological Emotional state Motor function	Aroclor 1016 Aroclor 1242 Aroclor 1254 Aroclor 1260	Mixture
relative brain weight, brain gross pathology and histopathology	Brain-histological, structural, morphological	Aroclor 1242	Mixture
brain weight	Brain-histological, structural, morphological	Aroclor 1242 Aroclor 1254	Mixture
brain weight sex-specific behavior (sweet preference test)	Brain-histological, structural, morphological Emotional state	Aroclor 1254 Breast milk mixture: PCBs 28, 77, 101, 105, 118, 126, 138, 146, 153, 156, 169, 170, 180, 187	Mixture

	Rhesus monkey	Macaca Mulatta	Oral-diet
	Rat	Sprague-Dawley	Oral-gavage
	Rat	Sprague-Dawley	Oral-diet
	Rat	Sprague-Dawley	Oral-diet
	Swine	mixed breed	Oral-diet
	Sheep Swine	Western crossbred feeder lambs Crossbred feeder pig	Oral-diet
	Rat	Long-Evans	Oral-diet

only animals from the 2.5ppm group survived for testing. Many tests were far removed from developmental exposure; Tests were correlated to PCB body burdens over time.  
Study also reports on conception rate, infant mortality, birth weight, and dermal and ocular effects; these findings were first reported by HERO #66483

study also evaluated spontaneous vocalizations, fecal boli production, and startle response but did not report the results

ADME data includes PCB residues in the brain

focus of study on growth and GI lesions

Herr et al.	1996	202323	2205110	no	N/A
Hornshaw et al.	1986	202328	2207219	No	N/A
Iatropoulos et al.	1978	202339		no	N/A
Kihlström et al.	1992	202369		no	N/A
Morse et al.	1996	202450		no	N/A
Nishida et al.	1997	202460		no	N/A
Provost et al.	1999	202486		no	N/A
Seegal et al.	1986	202527		no	N/A
Ward	1985	202585		no	N/A
Villeneuve et al.	1971	202651		no	N/A
Seegal et al.	1992	202763		no	N/A
Brezner et al.	1984	202791		no	N/A
Corey et al.	1996	202841		no	N/A
Altmann et al.	2001	594585	2151845	no	N/A

brainstem auditory evoked responses, cochlear and auditory function	Sensory function	Aroclor 1254	Mixture
listlessness, nervousness	Neurological symptoms	Aroclor 1254	Mixture
central nervous system histopathology severe depression/ataxia	Brain-histological, structural, morphological Motor function	Clophen A30	Mixture
brain weight	Brain-histological, structural, morphological	Aroclor 1254 Clophen A50	Mixture
brain weight	Brain-histological, structural, morphological	Aroclor 1254	Mixture
flavor aversive conditioning (saccharin preference) motor activity	Cognitive-behavioral tests Motor function	Aroclor 1254	Mixture
spatial learning in the Morris water maze	Cognitive-behavioral tests	Aroclor 1254	Mixture
concentrations of dopamine (DA) and its major metabolites in caudate nucleus and lateral olfactory tract	Neurotransmitter levels	Mixture: Aroclors 1254, 1260	Mixture
brain histopathology	Brain-histological, structural, morphological	Aroclor 1254	Mixture
brain weight	Brain-histological, structural, morphological	Aroclor 1254	Mixture
regional brain dopamine concentrations	Neurotransmitter levels	Aroclor 1016 Aroclor 1260	Mixture
maternal behavior	Social behavior	Aroclor 1254	Mixture
radial arm maze memory testing	Cognitive-behavioral tests	Aroclor 1254	Mixture
long term potentiation (LTP) in the visual cortex and hippocampus	Neurophysiology	Aroclor 1254 Breast milk mixture: PCBs 28, 77, 101, 105, 118, 126, 138, 146, 153, 156, 169, 170, 180, 187	Mixture

	Rat	Long-Evans	Oral-gavage
	Mink	Mustela Vison	Oral-diet
	Rhesus monkey	Macaca Mulatta	Oral-gavage
	Mink	Standard breed	Oral-diet
	Rat	Wistar	Oral-gavage
	Rat	Long-Evans	Oral-gavage
	Rat	Sprague- Dawley	Oral-diet
	Rat	Wistar	Oral-gavage
	Rat	F344	Oral-diet
	Rabbit Rat	Not reported Wistar	Oral-diet Oral-gavage
	Pigtail monkey	Macaca Nemestrina	Oral-cookie
	Rat	Wistar	Oral-gavage
	Rat	Sprague- Dawley	Oral-diet
	Rat	Long-Evans	Oral-diet

same animals from Goldey 1995b; brainstem auditory evoked responses assessed at about 1 year old

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The saccharin preference test is considered cognitive for this study because the authors specifically used it in a paired conditioning paradigm, which is largely cognitive.

ADME- also includes brain measurements by congeners

ADME data included PCB residues in the brains of dams, fetuses, and pups

unique exposure set up- exposed during different windows of conception, weaning, and 60 days of age

estimates of food intake data are provided. Recordings provided in females (hero ID XX reports male data)



Kostyniak et al.	2005	595287		no	N/A
Dziennis et al.	2008	604867		no	N/A
Colciago et al.	2009	625490		no	N/A
Zahalka et al.	2001	625812		no	N/A
Seegal et al.	2002	625951		no	N/A
Meerts et al.	2004	626549		no	N/A
Gilbert et al.	2000	626689		no	N/A
Powers et al.	2006	626887		no	N/A

brain weight	Brain-histological, structural, morphological	Fox River PCB mixture	Mixture
sensitivity to ischemic brain injury	Brain-histological, structural, morphological	Aroclor 1254	Mixture
Morris water maze (spatial memory) passive avoidance, forced swimming test (depression), elevated zero maze test (anxiety) locomotor activity	Cognitive-behavioral tests Emotional state Motor function	Mixture: PCBs 126, 138, 153, 180	Mixture
brain weight and weight of various brain regions spatial learning and memory using t-maze delayed alternation and Morris water maze tasks dopamine and norepinephrine levels in 6 brain regions	Brain-histological, structural, morphological Cognitive-behavioral tests Neurotransmitter levels	Aroclor 1016 Aroclor 1254	Mixture
dopamine levels in dialysates (extra neuronal DA) from the striatum	Neurotransmitter levels	Aroclor 1254	Mixture
passive avoidance open field testing dopamine and serotonin metabolites auditory thresholds (brain stem auditory evoked potentials BAEPS)	Emotional state Motor function Neurotransmitter levels Sensory function	Aroclor 1254	Mixture
swim speed (Morris water maze) spatial learning (Morris water maze) electrophysiology	Cognitive-behavioral tests Motor function Neurophysiology	Aroclor 1254	Mixture
auditory assessment using distortion product otoacoustic emissions (DPOAE) to assess ototoxicity and cochlear function	Sensory function	Fox River PCB mixture	Mixture

	Rat	Long-Evans	Oral-cookie
	Rat	Wistar	Oral-cookie
	Rat	Sprague-Dawley	Injection-sc
	Rat	Long-Evans	Oral-gavage
	Rat	Sprague-Dawley	Oral-cookie
	Rat	Wistar	Oral-gavage
	Rat	Long-Evans	Oral-gavage
	Rat	Long-Evans	Oral-cookie

When offspring reached 225–275 g body weight (6–8 weeks for males; 8–10 weeks for females), we induced transient focal cerebral ischemia
More severe effects with AR1254, but no behavioral effects observed with either treatment.
Evaluated brain weight, but did not report results
may be useful for susceptibility section (amphetamine)

Nguon et al.	2005	629930		no	N/A
Roegge et al.	2004	629932		no	N/A
Widholm et al.	2004	629934		no	N/A
Chu et al.	2008	652364		no	N/A
Berger et al.	2001	656205		no	N/A
Sable et al.	2006	656578		no	N/A
Sable et al.	2009	656579		no	N/A
Storm et al.	1981	657868	2199838	no	N/A
Lu et al.	2009	758055		No	N/A

cerebellar mass righting time, negative geotaxis, rotarod, startle response startle response	Brain-histological, structural, morphological Motor function Sensory function	Aroclor 1254	Mixture
brain weight motor testing: rope climb, parallel bars, rotating rod	Brain-histological, structural, morphological Motor function	Aroclor 1254	Mixture
series of spatial alternation tasks (cued spatial alternation) CA, noncued spatial alternation (NCA), and delayed spatial alternation (DSA) using standard 2-lever operant testing chambers	Cognitive-behavioral tests	Aroclor 1254	Mixture
brain weight, brain histopathology	Brain-histological, structural, morphological	Aroclor 1254	Mixture
fixed interval presses, transition bursts fixed interval presses, response bursts, transition presses	Cognitive-behavioral tests Emotional state	Aroclor 1248	Mixture
differential reinforcement of high rate (DRH) operant task, DRL responses	Cognitive-behavioral tests	Fox River PCB mixture	Mixture
brain body weight ratio operant task of timing and inhibitory control using differential reinforcement low rate operant tasks	Brain-histological, structural, morphological Cognitive-behavioral tests	Fox River PCB mixture	Mixture
conditioned avoidance response training open field testing	Emotional state Motor function	Aroclor 1254	Mixture
activity suppression	Motor function	Aroclor 1254	Mixture

	Rat	Sprague-Dawley	Oral-syringe
	Rat	Long-Evans	Oral-cookie
	Rat	Long-Evans	Oral-cookie
	Rat	Sprague-Dawley	Oral-cookie
	Rat	Sprague-Dawley	Oral-diet
	Rat	Long-Evans	Oral-cookie
	Rat	Long-Evans	Oral-cookie
	Mouse	ICR	Oral-diet
	Rat	CHECK	Oral-gavage

<p>Assessed motor behavior using rotating rod, vertical rope climbing, and parallel bar tests.  Also evaluated coexposures with MeHg. Dosing performed using spiked cookies.  Assessed both male and female offspring</p>
<p>also evaluated coexposures with MeHg. Dosing performed using spiked cookies. One male and one female  form each litter tested (PND 110).</p>
<p>dose administered needs some extrapolation; also feeding occurred following a 23 hour fast- animal stress  concerns?</p>
<p>Dosing performed using spiked cookies.  at PND 235 tested on differential reinforcement of high rate operant task (DRH), testing on differential  reinforcement of low rate operant task (DRL). Extinction measured inter response times. Researched  observed deficits in inhibitory control</p>
<p>also evaluated coexposures with MeHg. Dosing performed using spiked cookies.</p>



Yang et al.	2009	758056		no	N/A
Tewari et al.	2009	758057		no	N/A
Branchi et al.	2002	787645		no	N/A
Pereira et al.	2007	789165		no	N/A
Pereira and Rao	2007	789216		No	N/A
Jonsson et al.	1975	1061281	2198717	No	N/A
Lee et al.	2012	1293792		no	N/A
Poon et al.	2011	1293944		no	N/A
Lilienthal et al.	2006	1298501		no	N/A
Shiota	1976	1300832		no	N/A
Seegal et al.	1985	1303483		no	N/A
Pereira and Rao	2006	1313222		No	N/A

Brain histopathology Morris water maze (escape latency, animal reach criterion)	Brain-histological, structural, morphological Cognitive-behavioral tests	Aroclor 1254	Mixture
righting reflex	Motor function	Aroclor 1254	Mixture
open field test, ultrasonic vocalizations modified Fox battery: righting reflex, forelimb stick grasp reflex, forelimb placing reflexes, vertical screen test, screen climbing test, pole grasping, negative geotaxis, homing test	Emotional state Motor function	Aroclor 1254	Mixture
sluggishness and lethargic behavior	Neurological symptoms	Clophen A60	Mixture
motor activity	Motor function	Clophen A60	Mixture
animals mated	Social behavior	Aroclor 1242	Mixture
locomotor activity striatal dopamine levels	Motor function Neurotransmitter levels	Aroclor 1254	Mixture
brain weight DPOAE amplitudes	Brain-histological, structural, morphological Sensory function	Fox River PCB mixture	Mixture
brain weight sweet preference	Brain-histological, structural, morphological Emotional state	Aroclor 1254	Mixture
water T-maze test open field test	Cognitive-behavioral tests Emotional state	Kanechlor 500	Mixture
Urinary homovanillic acid concentrations	Neurotransmitter levels	CHECK	Mixture
sluggish and lethargic	Neurological symptoms	Clophen A60	Mixture

	Rat	Long-Evans	Oral-cookie
	Mouse	C57BL/6	Injection-ip
	Mouse	CD-1	Oral-gavage
	Rat	Albino Wistar	Oral-diet
	Rat	Wistar	Oral-diet
	Rat	Sprague-Dawley	Oral-diet
	Mouse	C57BL/6	Oral-cookie
	Rat	Long-Evans	Oral-cookie
	Rat	Long-Evans	Injection-sc
	Rat	Sprague-Dawley	Oral-gavage
	Rat	Wistar	Oral-gavage
	Rat	Wistar	Oral-diet

also includes some invitro mechanistic data about RyR and PCB-95 & PCB-66 specifically. Also includes PCB congener levels in brain tissue- ADME Assessed both male and female offspring
same study evaluated BDE-99
One-generation reproductive toxicity study with PCB or mixture with diethyl phthalate
the test substance was incorporated into a vanilla wafer cookie; ADME data includes PCB congener profiles in brain tissues; other MOA data included oxidative stress-related protein expression in the striatum and cerebellum and iron regulatory protein expression in the brain
Study looking at effects of PCB or mixture of PCB and diethyl phthalate on female rats

Elnar et al.	2012	1323584		no	N/A
Bavithra et al.	2012	1402037		no	N/A
Curran et al.	2011	1402199		no	N/A
Tian et al.	2011	1402374		no	N/A
Curran et al.	2011	1402788		no	N/A
Koller and Zinkl	1973	1404476		no	N/A

Morris water maze elevated plus maze, light dark box, open field forelimb grip strength, water escape pole climbing, negative geotaxis maternal behavior	Cognitive-behavioral tests Emotional state Motor function Social behavior	Mixture: PCBs 28, 52, 101, 138, 153, 180	Mixture
cerebellar histopathology	Brain-histological, structural, morphological	Aroclor 1254	Mixture
long-term potentiation, brain histopathology novel object recognition, Morris water maze elevated zero maze, acoustic startle response w/prepulse inhibition (PPI) open field activity neurotransmitters	Brain-histological, structural, morphological Cognitive-behavioral tests Emotional state Motor function Neurotransmitter levels	Mixture: PCBs 77, 105, 118, 126, 138, 153, 169, 180	Mixture
novel object test, Y-maze test elevated plus maze test, open field test	Cognitive-behavioral tests Emotional state	Aroclor 1254	Mixture
brain histology	Brain-histological, structural, morphological	Mixture: PCBs 77, 105, 118, 126, 138, 153, 169, 180	Mixture
Brain weight and histopathology	Brain-histological, structural, morphological	Aroclor 1221 Aroclor 1242 Aroclor 1254	Mixture

	Mouse	Swiss albino	Oral-gavage
	Rat	Wistar	Injection-ip
	Mouse	C57BL/6J (B6) B6.D2-Ahrd Cyp1a2 knockout	Oral-gavage
	Mouse	ICR	Oral-gavage
	Mouse	C57BL/6J (B6)	Oral-gavage
	Rabbit	New Zealand White	Oral-gavage

MOA info on mRNA expression of brain receptors and NT changes

Group I was vehicle control, Group II received Aroclor 1254 by injection, Group III received Aroclor 1254 by injection and quercetin (50 mg/kg/d) by gavage, Group IV received quercetin alone

Cannot locate number of dams exposed; data only provided on offspring/litter sizes

RT-PCR used to measure mRNA levels

At GD11.5, two whole embryos were pooled for analysis. At GD18.5, brain (pooled from two fetuses) and liver (from a single fetus) were analyzed. Adipose samples from PND6 litters, as well as PND13 litters, were pooled, using both subcutaneous fat and inguinal fat pad. At PND28, there was sufficient adipose tissue available to analyze subcutaneous fat and the inguinal fat pad separately

only mention that brains were collected and weighed but do not report the data in the text or results section



Platonow et al.	1976	1405279		no	N/A
Oishi et al.	1978	1405559		no	N/A
Mele et al.	1986	1408333	2207205	no	N/A
Sugawara et al.	2008	1410853		no	N/A
Seegal	1994	1411680	2183782	no	N/A
Chung and Clemens	1999	1414725		no	N/A
Pruitt et al.	1999	1414981		no	N/A
Geller et al.	2001	1415790		no	N/A

brain histopathology	Brain-histological, structural, morphological	Aroclor 1232 Aroclor 1242 Aroclor 1254	Mixture
absolute and relative brain weight, gross pathology of brain	Brain-histological, structural, morphological	Kanechlor 500	Mixture
operant conditioning (fixed-interval schedule of food reinforcement, reinforcement omission procedure)	Cognitive-behavioral tests	Aroclor 1248	Mixture
brain histopathology water maze test open-field test grasp reflex, righting reflex, walking, negative geotaxis, cliff avoidance, spontaneous locomotion activity, swimming speed	Brain-histological, structural, morphological Cognitive-behavioral tests Emotional state Motor function	Aroclor 1254	Mixture
neurotransmitter levels	Neurotransmitter levels	Aroclor 1016 Aroclor 1254 Aroclor 1260	Mixture
Female sexual behavior (pacing test), not including lordosis	Social behavior	Aroclor 1221 Aroclor 1254	Mixture
histological/morphological changes in hippocampal mossy fibers	Brain-histological, structural, morphological	Aroclor 1254	Mixture
operant conditioning visual thresholds, electroretinography for retinal physiology	Cognitive-behavioral tests Sensory function	Aroclor 1254	Mixture

	Swine	Yorkshire	Oral-diet
	Rat	Sprague-Dawley	Oral-diet
	Rhesus monkey	Macaca Mulatta	Oral-diet
	Mouse	C57BL/6Cr	Oral-gavage
	Pigtail monkey Rat	Macaca Nemestrina Wistar	Oral-cookie Oral-diet
	rat	Long-Evans	Injection-ip
	Rat	Sprague-Dawley	Oral-diet
	Rat	Long-Evans	Oral-gavage

<p>additional exposure group, females fed 0.5 ppm PCBs in diet three times per week for 18 months, from unknown starting time through weaning of infants at 4 months old</p> <p>Why isn't this group included as an entry in the inventory?</p>
<p>this study also examined the neurobehavioral effects of coexposure to MeHg and Aroclor 1254</p>
<p>female offspring were ovariectomized and administered estradiol followed by progesterone to bring them into sexual receptivity; behavioral tests began 4 hrs after progesterone treatment; hormone-treated females were tested for sexual behavior once per week for five weeks from day 70-105; 25 females were sacrificed after the last behavior test and tyrosine hydroxylase immunoreactivity was used to identify dopaminergic neurons in the caudal incertohypothalamic region</p>
<p>neurotransmitter data also collected- maybe reported in a sister paper?</p>

Sugawara et al.	2006	1416422		no	N/A
Chung et al.	2001	1416578		no	N/A
Herr et al.	2001	1416693		no	N/A
Taylor et al.	2002	1417198		no	N/A
Nakai et al.	2005	1417552		no	N/A
Salama et al.	2003	1418293		no	N/A
Khan and Thomas	2004	1418852		no	N/A

<p>Morris water maze test</p> <p>open-field test</p> <p>grasp reflex, righting reflex, walking, negative geotaxis, cliff avoidance, spontaneous locomotion activity</p>	<p>Cognitive-behavioral tests</p> <p>Emotional state</p> <p>Motor function</p>	Aroclor 1254	Mixture
<p>Female sexual behavior (pacing test), not including lordosis</p>	Social behavior	<p>Aroclor 1221</p> <p>Aroclor 1254</p>	Mixture
<p>visual-evoked potentials (flash-evoked potentials), somatosensory-evoked potentials (SEP<sub>cortex</sub> and SEP<sub>cerebellum</sub>), peripheral nerve-evoked potentials (compound nerve action potential and nerve conduction velocity-evoked potentials), low-frequency auditory function (reflex modification audiometry)</p>	Sensory function	Aroclor 1254	Mixture
<p>schedule-controlled behavior: acquisition and steady-state performance under a series of fixed-interval reinforcement schedules</p>	Cognitive-behavioral tests	Aroclor 1254	Mixture
<p>brain weight</p> <p>neurotransmitter levels</p>	<p>Brain-histological, structural, morphological</p> <p>Neurotransmitter levels</p>	Aroclor 1254	Mixture
AVPV and SON volume	Brain-histological, structural, morphological	Aroclor 1221	Mixture
<p>serotonin (5-HT) concentrations in the brainstem and frontal cortex</p>	Neurotransmitter levels	Aroclor 1254	Mixture

	Mouse	C57BL/6Cr	Oral-gavage
	Rat	Long-Evans	Injection-ip
	Rat	Long-Evans	Oral-gavage
	Rat	Long-Evans	Oral-gavage
	Rat	Sprague-Dawley	Oral-gavage
	Rat	Sprague-Dawley	Injection-ip
	Rat	Sprague-Dawley	Oral-gavage

Study performed a developmental exposure (postnatal exposure) but also examined effects in 60 day old females with no postnatal exposure (to separate concurrent from stored PCB effects)
assessed at 128–140 days of age
This study also contains results on ER-beta cell number in the anteroventral periventricular nucleus. Other outcomes: age at vaginal opening, age at first estrus, non-significant increase in combined uterine and ovarian weight,
contains PCB brain concentrations- ADME



Selvakumar et al.	2013	2149762		no	N/A
Poon et al.	2013	2149921		no	N/A
Pratheepa Kumari et al.	2011	2151606		no	N/A
Branchi et al.	2005	2155131		no	N/A
Chu et al.	2005	2157748		no	N/A
Muthuvel et al.	2006	2159859		no	N/A
Fanini et al.	1990	2172957		no	N/A
Seegal et al.	1985	2175561	2198848	no	N/A
Schmoldt et al.	1977	2179041		no	N/A
Allen et al.	1976	2179602		no	N/A
Itokawa et al.	1975	2180042		no	N/A

brain histopathology learning and memory in the 8-arm radial maze open field test plasma neurotransmitter levels	Brain-histological, structural, morphological Cognitive-behavioral tests Emotional state Neurotransmitter levels	Aroclor 1254	Mixture
locomotor activity (beam breaks)	Motor function	Fox River PCB mixture	Mixture
brain histology	Brain-histological, structural, morphological	Aroclor 1254	Mixture
open field activity	Emotional state	Aroclor 1254	Mixture
brain weight	Brain-histological, structural, morphological	Aroclor 1254	Mixture
hypothalamus weight	Brain-histological, structural, morphological	Aroclor 1254	Mixture
exploratory activity traction, rotarod, spontaneous motor activity aggressive behavior, social activity, indifference	Cognitive-behavioral tests Motor function Social behavior	Fenclo 54	Mixture
regional brain differences in norepinephrine levels	Neurotransmitter levels	Mixture: Aroclors 1254, 1260	Mixture
brain weight	Brain-histological, structural, morphological	Clophen A30	Mixture
brain weight	Brain-histological, structural, morphological	Aroclor 1242 Aroclor 1254 Aroclor 1262	Mixture
brain weight and histopathology	Brain-histological, structural, morphological	Kanechlor 500	Mixture

	Rat	Wistar	Injection-ip
	Rat	Long-Evans	Oral-cookie
	Rat	Wistar	Injection-ip
	Mouse	CD-1	Oral-gavage Oral-syringe
	Rat	Sprague-Dawley	Oral-cookie
	Rat	CHECK	Injection-ip
	Mouse	Not reported	Injection-ip Oral-diet
	rat	Wistar	Oral-gavage
	rat	Wistar	Oral-diet
	Rat	Sprague-Dawley	Oral-diet
	Rat	Wistar	Oral-diet

<p>also evaluated BDE-99</p> <p>Also evaluated brain weight, but did not report the results</p>
<p>Main focus of the paper is an organochlorine mixtures study, AR1254 used as a positive control</p>
<p>MOA only, assess the effect of antioxidant treatment on the amelioration of PCB-induced oxidative stress in the brain</p>
<p>some animals were housed for 21 days in dark prior to behavioral testing- is this standard?</p>

Seegal et al.	1991	2183795		no	N/A
Villeneuve et al.	1971	2187123	2181176, 2199350	no	N/A
National Cancer Institute	1978	2192571		no	N/A
Grant et al.	1972	202477	2204253	no	N/A
Reilly et al.	2015	2919758		no	N/A
Meyer et al.	2015	2919792		no	N/A
Poon et al.	2015	2920043		no	N/A

reduction of dopamine content in the brain	Neurotransmitter levels	Aroclor 1016	Mixture
brain weight	Brain-histological, structural, morphological	Aroclor 1221 Aroclor 1254	Mixture
brain histopathology tremors activity level	Brain-histological, structural, morphological Motor function Neurological symptoms	Aroclor 1254	Mixture
brain weight	Brain-histological, structural, morphological	Aroclor 1221 Aroclor 1254	Mixture
sociability/novelty	Social behavior	Aroclor 1221	Mixture
pup relative brain weight inhibitory control performance: differential reinforcement of low rates (DRL) 15 performance (ratio of reinforced:nonreinforced lever presses and reinforcers earned)	Brain-histological, structural, morphological Cognitive-behavioral tests	Fox River PCB mixture	Mixture
audiogenic seizures	Sensory function	Fox River PCB mixture	Mixture

	Pigtail monkey	Macaca nemestrina	Oral-gavage
	Rabbit	Not reported	Oral-gavage
	Rat	Fischer 344	Oral-diet
	Rat	Wistar	Oral-diet
	Rat	Sprague- Dawley	Injection-ip
	Rat	Long-Evans	Oral-cookie
	Rat	Long-Evans	Oral-cookie

"Ortho-substituted, non-planar PCBs reduce dopamine content in both nonhuman primate brain and pheochromocytoma (PC12) cells. Planar, dioxin-like, congeners have no effect on dopamine content in PC 12 cells. Additional in-vitro results indicate that dopamine reduction by PCBs is due to inhibition of tyrosine hydroxylase activity." NOTE that in vitro experiments were performed with individual congeners and mixtures of congeners. There is some accumulation data for PCB congeners in vitro (review for ADME)

Note: Paper states orally administered. Gavage assumed.

Also evaluated open field behavior, elevated plus maze, fear conditioning, and mate preference, but did not report results

a stock solution of the Fox River PCB mixture (Kostyniak et al., 2005) was diluted with corn oil and pipetted onto a vanilla wafer cookie; behavioral training and testing began when the pups were 100 days old; this study also examined the effects of microinjections of the dopamine agonists bupropion, quinpirole, and SKF81297 directly into the medial prefrontal cortex (mPFC) on inhibitory control performance in adult rats that were perinatally exposed to PCBs



Naveau et al.	2014	2920420		no	N/A
Nam et al.	2014	2920493		no	N/A
Hu et al.	2015	3005022		no	N/A
Lombardo et al.	2015	3007891		no	N/A
Folland et al.	2015	3063353		no	N/A
Elnar et al.	2016	3121413		no	N/A
Bandara et al.	2016	3350985		no	N/A
Sumathi et al.	2016	3351130		no	N/A
Tang et al.	2015	3351160		no	N/A
Wahlang et al.	2016	3351296		no	N/A

fetal cerebral cortex development: neuronal progenitor proliferation, cell cycle exit, differentiation rate, cell death, radial migration, and cortical laminar organization	Brain-histological, structural, morphological	Aroclor 1254	Mixture
novel object recognition elevated plus maze, open field	Cognitive-behavioral tests Emotional state	Aroclor 1254	Mixture
brain weight and histopathology	Brain-histological, structural, morphological	Chicago Air Mixture + PCB 11	Mixture
operant conditioning hyperactivity	Cognitive-behavioral tests Emotional state	Aroclor 1248	Mixture
brain weight	Brain-histological, structural, morphological	Aroclor 1268	Mixture
short-term spatial memory (Y-maze)	Cognitive-behavioral tests	Mixture: PCBs 28, 52, 101, 138, 153, 180	Mixture
audiogenic seizures	Sensory function	Fox River PCB mixture	Mixture
brain histopathology spatial memory (MWM), radial arm maze open field activity muscle grip strength (rotarod)	Brain-histological, structural, morphological Cognitive-behavioral tests Emotional state Motor function	Aroclor 1254	Mixture
righting reflex, cliff drop test response, negative geotaxis	Motor function	Aroclor 1254	Mixture
activity level	Motor function	Aroclor 1260	Mixture

	rat	Wistar	Oral-cookie
	Mouse	ICR	Oral-gavage
	Rat	Sprague-Dawley	Inhalation
	rat	Sprague-Dawley	Inhalation
	Mink	Mustela Vison	Oral-diet
	Mouse	swiss albino	Oral-gavage
	Rat	Long-Evans	Oral-cookie
	rat	albino	Injection-ip
	Mouse	ICR	Oral-gavage
	Mouse	C57Bl/6J	Oral-gavage

test substance was injected into a wafer that was fed to the dams; ADME data included PCB congener analysis in the fetal brain

only brain weight (no sig difference) is reported

also evaluated long-term spatial learning and memory using the Morris water maze in PCB-treated animals, but only after intracerebroventricular injection of amyloid beta oligomers

Bell et al.	2016	3351306		no	N/A
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<p>elevated plus maze and light-dark box (anxiety)</p> <p>sociosexual interactions, ultrasonic vocalizations and affiliative behavior, sociability</p>	<p>Emotional state</p> <p>Social behavior</p>	<p>Aroclor 1221</p>	<p>Mixture</p>
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	Rat	Sprague-Dawley	Injection-ip
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Although sociosexual interactions were evaluated in this study, due to the nature of the observed responses, they are classified as social behavior rather than sexual behavior: "Prenatal exposure increased the number of flat calls in the session preceding the opposite sex interaction in males, independent of juvenile exposure...Other aspects of USV behavior with an opposite sex conspecific were unaffected by treatments...Males exposed to PCBs prenatally spent less time near a no-hormone stimulus animal than animals not exposed prenatally, independent of juvenile exposure...As no significant effects were seen on time spent near a hormone stimulus animal...this effect drove the preference for a hormone-treated stimulus animal in prenatally exposed males...Juvenile exposed males spent more time with the no-hormone female than did unexposed males...This effect, together with the nonsignificant increase in time spent with the hormone-treated stimulus females, resulted in the observation that males with juvenile exposure spent more time with both stimulus animals than males not exposed at that time..."



Wahlang et al.	2017	3982706		no	N/A
Gillette et al.	2017	3982717		no	N/A

physical activity	Motor function	Aroclor 1260	Mixture
elevated plus maze and light-dark box (anxiety)	Emotional state	Aroclor 1221	Mixture

	Mouse	C57Bl/6	Oral-gavage
	Rat	Sprague-Dawley	Injection-ip

One comparison group was dosed with a single PCB congener (PCB 126); there was an appropriate negative control group (corn oil).

Authors compare animals fed an amino acid control diet to those fed a methionine-choline deficient diet: "For the first two weeks, all animals received the amino acid control diet (CD;TD.94149; Harlan Teklad, Madison, WI, USA). Diet components are described in Supplementary Table 1. The groups designed to receive the methionine-choline deficient (MCD) diet were fed with the MCD diet (TD.90262, Harlan Teklad) from week 3 onwards. On week 6–7 and week 8–9, the MCD-fed mice were restored back to CD-feeding because of the excess weight loss that was noncompliant with the IACUC protocol."

"...Animals were gavaged in two individualized doses on week 5 and week 7 to minimize acute toxicity, resulting in a cumulative dosage of 4.9 mg/kg for PCB 126 and 20 mg/kg for Aroclor 1260."  
"After the second gavage was administered (week 7), some of the mice from the MCD + PCB 126 group died (n = 3). The rest of the mice were extremely sick and lethargic, and their body weight was under the weight limit required by the IACUC protocol (>20% loss in body weight), hence they were subsequently euthanized at the end of week 8. Due to their extremely low bodyweight, only their livers were collected for hepatic analysis."

Methodology evaluation: authors fail to adequately account for extraneous variables introduced by malnourishment of methionine-choline-deficient group.

Relevant to MOA for hepatic, cardiac and metabolic effects.

Hepatic: gluconeogenic enzyme expression [Pepck-1 and G6Pase], target genes of hepatic receptors [Cyp1a2, Fmo3 (AhR targets), Cyp2b10 (CAR target) and Cyp3a11 (PXR target)], genes involved in fatty acid metabolism [Pparalpha, Cypt1a, Cd36], and genes involved in cell survival and anti-oxidation [Fas, Nqo1, Hmox-1].

Cardiac: plasma levels of early markers of endothelial dysfunction [ICAM-1, Pecam-1, P-Selectin and thrombomodulin] and gene markers of heart injury [Fgf21, ANF].

Metabolic: HOMA-b, a marker of pancreatic cell function, leptin and resistin [adipokines].

Identified in targeted literature search (cognitive effects, affective and social behavior)

Body weights were measured during pre-puberty, adolescence, and adulthood. Listed prepubertal and adolescent weights under developmental effects. Listed adult body weights under metabolic effects.

Seeking EPA review for categorization of this study.

Sadowski et al.	2016	3983596		no	N/A
Monaikul et al.	2017	3983676		No	N/A

activation of auditory cortex	Neurophysiology	Fox River PCB mixture	Mixture
operant behavior	Cognitive-behavioral tests	Fox River PCB mixture	Mixture

	Rat	Long-Evans	Oral-cookie
	Rat	Long-Evans	Oral-syringe

Nervous system effects are the activation/development of the auditory cortex. Mothers were exposed orally through diet, but outcomes were measured for grown offspring (brain slices). There were significant increases in the ratio of aCSF/SR95531 activation in slices from PCB-exposed animals compared to control animals.

Relevant to MOA for neurological effects. The authors used GABA and NMDA receptor antagonists to explore excitatory and inhibitory neurotransmitters affected by PCBs in the auditory cortex.

Identified in targeted literature search (cognitive effects, affective and social behavior)

Cognitive function was measured by cognitive flexibility, response inhibition. There were subtle sex-specific effects of PCB exposure in adolescent rats on the reversal phase of a set-shifting task, but no effects of exposure on performance on a DRL15 task, suggesting an effect on cognitive flexibility but not response inhibition.



Mucio-Ramírez et al.	2017	3984423		no	N/A
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brain histopathology	Brain-histological, structural, morphological	Aroclor 1254	Mixture
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	Rat	Wistar	Oral-cookie
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This is primarily a mechanistic study that examines osmotic regulation due to alterations in hypothalamic vasopressin expression in Aroclor 1254 treated mice. Authors conduct osmoregulatory challenge (salt loading) listed under endocrine effects. This study also includes cell counts in paraventricular (PVN) and supraoptic nuclei (SON) of the hypothalamus which could be listed as neurological effects. However, because this data is in support of the endocrine effects, we listed this as MOA information in support of endocrine effects. ICF is requesting EPA review for including only endocrine effects for this study.

Relevant to MOA for endocrine effects. The authors report information on the gene expression and immunoreactivity of vasopressin and gene expression of cFOS. The results showed significant reduction in vasopressin reactive neurons, and vasopressin mRNA expression as compared to the hyperosmotic controls.

Authors suggest that "Aroclor 1254 may interfere with the activation of vasopressin mRNA transcript levels and protein, causing a central dysfunction of vasopressinergic system." Authors also found that "cFOS mRNA expression increased in Aroclor 1254 dehydrated groups, suggesting that the decrease [in vasopressin immunoreactivity] was not due to a lack of the response to the osmotic activation [in neuroendocrine cells of the hypothalamus]."

Miller et al.	2017	3984651		No	N/A
Miller et al.	2017	3985147		No	N/A

activity box	Motor function	Fox River PCB mixture	Mixture
operant testing	Cognitive-behavioral tests	Fox River PCB mixture	Mixture

	Rat	Long-Evans	Oral-cookie
	Rat	Long-Evans	Oral-cookie

Identified in targeted literature search (cognitive effects, affective and social behavior)

Only pre-cocaine injection is data of interest.

Administered mixture was 35% Aroclor 1242, 35% Aroclor 1248, 15% Aroclor 1254, and 15% Aroclor 1260.

Only behavior/activity data presented. Authors state, "In the interest of brevity only significant PCB exposure and sex related effects are presented."

Authors compare reproductive/hepatic data results to another study in the methods sections:

"Physiological measures including the dam liver weight, number of embryo implantation sites in the dam, and brain:body-weight, liver:body-weight and thymus:body-weight ratios in the pups were determined, as was the percent of gestational and lactational weight-gain in the dams and postnatal body weights of the pups on PND 0, 7, 14, and 21. These measures were very similar to what has previously been reported (Sable et al., 2011)." These authors did not report on these endpoints.

Identified in targeted literature search (cognitive effects, affective and social behavior)

Nervous system effects involved changes in intravenous self-administration (IV SA) of the psychostimulant cocaine due to perinatal exposure to a PCB mixture.

PCB exposure enhanced early cocaine drug-seeking in this preclinical model of developmental contaminant exposure (particularly in males), but no differences were seen during later cocaine SA sessions.



Bandara et al.	2017	3985418		no	N/A
Bavithra et al.	2017	3985422		No	N/A

seizure susceptibility	Neurophysiology	Fox River PCB mixture	Mixture
brain histopathology elevated plus maze, open field rotarod	Brain-histological, structural, morphological Emotional state Motor function	Aroclor 1254	Mixture

	Rat	Long-Evans	Oral-cookie
	Rat	Wistar	Injection-ip

Evaluated mixture consisting of 35% Aroclor 1242, 35% Aroclor 1248, 15% Aroclor 1254, and 15% Aroclor 1260; Measured seizure susceptibility based on electrical kindling from the amygdala.

In the PCB exposed pups, there were significant ( $p < 0.05$ ) decreases of 8, 13 and 19% in body weight compared to controls at postnatal days 7, 14 and 21. No other gross developmental abnormalities were noted. Body weight measures taken prior to and after the kindling procedure indicate that developmentally PCB exposed animals recovered to control body weights at adulthood ( $>PND\ 90$ ).

The neurophysiology endpoint was seizure susceptibility. This was measured by using the electrical kindling model - a model of epileptogenesis that is distinct from the audiogenic seizure model and primarily targets the limbic system as opposed to the auditory brainstem. Thus, this study explored a mechanistic model to study seizure susceptibility. However, even though these endpoints were on the mechanistic side, this study was classified as health effect, due to the direct applicability of the model. In the study, treated animals had attenuated focal (amygdala) excitability.

Identified in targeted literature search (cognitive effects, affective and social behavior)

One group was also treated with melatonin.

Relevant to MOA for neurological effects. The authors provided evidence that the impaired motor coordination in PCB treated rats was due to neurodegeneration in the motor cortex region (proapoptotic and antiapoptotic protein expressions and degenerative neurons in the cortical gray matter).

Parent et al.	2016	3985424		no	N/A
Klinefelter et al.	2018	4217253		no	N/A

<p>brain histopathology hippocampal development/neurophysiology</p>	<p>Brain-histological, structural, morphological Neurophysiology</p>	<p>Aroclor 1254</p>	<p>Mixture</p>
<p>brain histopathology (tyrosine hydroxylase optical staining in the striatum, cerebellar structure and cellular composition, cerebellar foliation)</p>	<p>Brain-histological, structural, morphological</p>	<p>Mixture: PCBs 77, 105, 118, 126, 138, 153, 169, 180</p>	<p>Mixture</p>

	Mouse	C57BL/6J	Oral-cookie
	Mouse	C57BL/6J	Oral-diet

This is primarily a mechanistic study relevant to neurological effects (PCB disruption of the functional synaptic development of newborn hippocampal granule cells). This study also measures T4 which was listed under endocrine health effects.

ICF included whole-cell recordings in brain slices prepared from the dentate gyrus to measure development of excitatory synapses under MOA in support of evaluating cognitive neurological effects. Although neurophysiological studies can be included as health effect data, we were not sure if this should be classified MOA because no cognitive function tests were conducted. ICF requests EPA review for including neurological effects.

Other Relevant MOA data for neurological effects included proliferation, survival and differentiation of neurons in the dentate gyrus (fluorescence microscopy to image GFP of newly generated granule cells (delivered by stereotactic retrovirus injection) and BRDU positive cells - BRDU also delivered by stereotactic injection). Study also evaluates spine density and morphology of granule cells in newborns and older mice.

Year should be 2018 not 2017

oral exposure through a dosed Froot Loop

Mixture preparation described in Curran et al. 2011a

Mouse genotypes: AhrbCyp1a2(+/+) and two knockout lines: high-affinity AhrbCyp1a2(-/-) and poor-affinity AhrdCyp1a2(-/-)

Has some TK info (marked ADME)

MOA: gene expression differences in cerebellum and cortex



Alcigir et al.	2018	4934444		no	N/A
Lombardo and Peck	2018	4985269		no	N/A
Karkaba et al.	2017	5017101		no	N/A
Topper et al.	2019	5880496		no	N/A
Krishnan et al.	2019	5880846		no	N/A

histopathological changes to neurons/brain (karyopyknosis, karyolysis, and cytoplasmic shrinkage)	Brain-histological, structural, morphological	Aroclor 1254	Mixture
ethanol consumption	Neurophysiology	Aroclor 1254 Aroclor 1260	Mixture
Social approach, social novelty	Social behavior	Mixture: PCBs 28, 52, 101, 138, 153, 180	Mixture
Sociosexual behavior	Social behavior	Aroclor 1221	Mixture
ultrasonic vocalizations (USVs), open field, light/dark box maternal behavior	Emotional state Social behavior	Aroclor 1221	Mixture

	Rat	Wistar	Oral-gavage
	Rat	Sprague-Dawley	Oral-cookie
	Mouse	CD1	Oral-diet
	Rat	Sprague-Dawley	Injection-ip
	Rat	Sprague-Dawley	

<p>Exposure from second week of gestation to postnatal day 21, daily, at 1 mg/kg/body weight in the dams.</p> <p>There was one control group and a third group co-exposed to PCBs and curcumin.</p> <p>MOA: gene expression, apoptosis, 8OHdG, 4HNE, MBP genetic expression in neurons; apoptosis (measured by DNA in situ fragmentation) in neurons; total antioxidant status and total oxidant status in nervous tissue homogenates; concentration of neuron-specific enolase in serum</p>
<p>Treatment was a 1:1 mixture of Aroclors 1254 and 1260</p>
<p>"Behavioral measurements were analyzed using three-way ANOVA, considering perinatal exposure to PCBs, sex, and age as independent between-subject fixed factors to compare experimental groups"</p> <p>"Study showed that PCBs altered several biochemical markers including corticosterone, revealing that PCB-exposed offspring males and females suffered from increased stress. Our results suggest that regular consumption of PCB-contaminated fish by pregnant and lactating women could disturb the formation of normal social habits in their offspring."</p> <p>MOA - myeloperoxidase (MPO) as a marker of inflammation</p>
<p>Measured Ultrasonic vocalizations.</p> <p>MOA-looked at neuroendocrine gene expression</p>
<p>This study appears is from the same group as HERO ID 5883620 (above); assessed the combinatorial impact of EDC-altered maternal care and transgenerational inheritance on F3 male and female offspring.</p>

Doğan and Alçıgır	2019	5881059		no	N/A
Hufgard et al.	2019	5882252		no	N/A
Reilly et al.	2018	5882811		No	N/A

histopathology of cerebral cortex and cerebellum	Brain-histological, structural, morphological	Mixture: PCB 28, PCB 47, PCB 77, PCB 126, Aroclor 1254, Aroclor 1260	Mixture
Morris water maze (MWM), fear conditioning open field, prepulse inhibition (sensorimotor gating) motor activity long-term potentiation in hippocampal tissue neurotransmitter levels acoustic startle response	Cognitive-behavioral tests Emotional state Motor function Neurophysiology Neurotransmitter levels Sensory function	Mixture: PCBs 77, 105, 118, 126, 138, 153, 169, 180	Mixture
Sociosexual behavior	Social behavior	Aroclor 1221	Mixture

	Rat	Wistar	Oral-gavage
	Mouse	Ahr^b1_Cy p1a2-/- KO C57BL6/J mice	Oral-gavage
	Rat	Sprague- Dawley	Injection-ip

The aims of this study were to examine the effects of prenatal Aroclor 1254 (PCBs mixture) exposure on central nervous system tissues DNA and to evaluate the effects of curcumin. Primarily mechanistic but also includes brain histopath of motor control regions.

"Study demonstrated that PCBs (Aroclor 1254) exposure in the prenatal period induces oxidative DNA damage in cerebral cortex and cerebellum. Plasma 8-(OH)DG concentrations could be used as a biomarker to evaluate the oxidative DNA damage caused by PCBs. Exogenous curcumin protects PCBs-induced DNA damage in the prenatal period. Finally, prenatal PCBs exposure induces the epigenetic changes in cerebral cortex and cerebellar DNA. However, further studies are needed to understand the long-term effects of increased cerebellar oxidative DNA damage and the protective effects of curcumin in PCBs exposure."

The study authors note that the PCB mixture used is environmentally relevant, and found in food, human tissues, and breast milk.

The study evaluates some MOA endpoints (gene expression and DNA methylation).

investigators used a more complex behavioral apparatus, an X-shaped Plexiglas apparatus (FourPlex), that enabled an experimental animal exposed to PCBs or a vehicle to distinguish and choose among 4 stimulus animals of the same or opposite sex, and of different hormonal status.



Colter et al.	2018	5882932		no	N/A
Krishnan et al.	2018	5883620		no	N/A

Motor function sensorimotor function	Motor function Sensory function	Mixture: PCBs 77, 105, 118, 126, 138, 153, 169, 180	Mixture
sexual behavior (USVs, paced behavior)	Social behavior	Aroclor 1221	Mixture

	Mouse	<p>3</p> <p>Genotypes:</p> <p>High-affinity Ahrb-Cyp1a2(+/+) wild type mice, two knockout lines used: AhrbCyp1a2 (-/-) and poor-affinity AhrdCyp1a2(-/-) (background strain C57BL/6J).</p>	Oral-gavage
	Rat	Sprague-Dawley	Injection-ip

Administration of PCBs included coplanar PCBs 77, 126, and 169 and noncoplanar PCBs 105, 118, 138, 153, 180. CYP1A1 induction confirmed in high-affinity Ahrb mice

Study examines intergenerational effects of various endocrine disruptors, including PCBs. Concludes that Exposure of rats to EDCs at the germ cell stage led to differences in the physiological and behavioral phenotype later in life, especially in males.

Author	Year	HERO ID	Redirect from	Exclude?	Standardized justification
Schantz et al. 1991	1991	17891		yes	Review
Goldey et al. 1995	1995	47251		no	N/A
Goldey et al. 1998	1998	51027		no	N/A

Endpoints Evaluated	Endpoint Category	Test compound
<p>2 choice discrimination learning reversal (1.5 yrs), delayed spatial alternation (4-6 yrs). Potential damage to prefrontal cortex- exposure from 0-4 months of age were never able to achieve control levels of performance on delayed spatial alternation task.</p>	Cognitive-behavioral tests	<p>Aroclor 1016 Aroclor 1248</p>
<p>motor development auditory startle response, auditory thresholds</p>	<p>Activity level/motor function Sensory function</p>	Aroclor 1254
<p>motor activity reflex modification audiometry</p>	<p>Activity level/motor function Sensory function</p>	Aroclor 1254

PCB Mixture or Congener?	t <sub>1/2</sub> (half-life of test compound in days)	Species	Strain	Primary exposure route (oral, inhalation, injection, dermal)
Mixture		Rhesus monkey	Macaca Mulatta	Oral-diet
Mixture		Rat	Long-Evans	Oral-gavage
Mixture		Rat	Long-Evans	Oral-gavage

<p><b>Exposure type:</b></p> <p><b>Primary:</b> Test compound directly administered to the animal evaluated for health effects</p> <p><b>Secondary:</b> Gestational and/or lactational exposures (even if animals are also exposed directly at some stages of the experiment)</p> <p><b>Primary, pre-weaning:</b> Test compound directly administered to animals during the nursing period; for these studies, enter <math>t_i(\text{start})</math> and <math>t_i(\text{end})</math></p>	<p><b>Primary exposures:</b></p> <p><math>t_m(\text{start})</math> (age of animal (in days) when dosing begins)</p>	<p><b>Primary exposures:</b></p> <p><math>t_m(\text{end})</math> (total exposure duration (in days))</p>	<p><b>Secondary exposure studies:</b></p> <p><math>n_i</math> (litter size)</p>	<p><b>Secondary exposures:</b></p> <p><math>t_m(\text{start})</math> (number of days after conception that dosing to dams begins)</p>
Secondary				
Secondary				6
Secondary				6



Secondary exposures: $t_m(\text{end})$ (number of days after conception that dosing to dams ends)	Secondary exposures and Primary exposures pre-weaning: $t_i(\text{start})$ (number of days after conception that dosing (direct - not via gestation or lactation) to offspring begins)	Secondary exposures and Primary exposures pre-weaning: $t_i(\text{end})$ (number of days after conception that dosing (direct - not via gestation or lactation) to offspring ends)	Dose as $\text{mg/kg}_{\text{bw}}/\text{d}$ (2) or $\text{mg/kg}_{\text{food}}$ (3)?	Lowest Dose Tested ( $\text{mg/kg}_{\text{bw}}/\text{d}$ or in $\text{mg/kg}_{\text{food}}$ ) - for secondary exposure studies, this represents the dose to the dam
			2	0.007 0.09
43			2	1
43			2	8

Highest Dose Tested (mg/kg <sub>bw</sub> /d or in mg/kg <sub>food</sub> ) - for secondary exposure studies, this represents the dose to the dam	NOAEL (mg/kg <sub>bw</sub> /d or in mg/kg <sub>food</sub> ) - for secondary exposure studies, this represents the dose to the dam	LOAEL: d <sub>m</sub> (mg/kg <sub>bw</sub> /d or in mg/kg <sub>food</sub> ) - for secondary exposure studies, this represents the dose to the dam	Secondary exposures and Primary exposures pre-weaning: LOAEL: d <sub>i</sub> (dose administered to offspring in mg/kg <sub>bw</sub> /d or in mg/kg <sub>food</sub> - this represents a direct dose - not via gestation or lactation; not every study will have this)	LOAEL (HED) (mg/kg-d)
8				
8				

**Notes on dosing estimates/calculations**

Author estimated Aroclor 1248 dose administered as  
0.09 mg/kg-day (reported in HERO ID #199761)



Lilienthal et al. 1991	1991	66506		no	N/A
Widholm et al. 2001	2001	103780		no	N/A
Gerstenberger et al. 2001	2001	116863		no	N/A
Hussain et al. 2000	2000	116866		yes	Evaluated only PCB mixtures with < 4 congeners
Lasky, RE; Widholm, JJ; Crofton, KM; Schantz, SL	2002	116876		no	N/A
Steinberg, RM; Juenger, TE; Gore, AC	2007	116896		no	N/A
Kodavanti et al. 1998	1998	130226		no	N/A
Bowers et al. 2004	2004	150620		no	N/A
Meerts et al. 2004	2004	150660		no	N/A
Amin, S, Moore, RW, Peterson, RE, et al.	2000	197169		yes	Evaluated only PCB mixtures with < 4 congeners

active avoidance learning (shuttle box) visual discrimination learning (lashley jumping stand and retention)	Emotional state Cognitive-behavioral tests	Clophen A30
spatial discrimination reversal learning (2 lever operant testing chambers)	Cognitive-behavioral tests	Aroclor 1254
surface righting, reflex suspension	Activity level/motor function	Aroclor 1016
		PCB 153
cochlear function (distortion product otoacoustic emissions), auditory evoked brain stem responses	Sensory function	Aroclor 1254
ambulation female sexual behavior: mating trial pacing, receptivity and proximity behaviors, avoidance/rejection behaviors	Activity level/motor function Sexual behavior	Aroclor 1221
motor activity in photocell neurochemical analysis of the cerebellum, frontal cortex, and striatum (norepinephrine, dopamine and their metabolites)	Activity level/motor function Neurotransmitter levels	Aroclor 1254
grip strength, righting reflex	Activity level/motor function	Aroclor 1254
brain weight	Brain-histological, structural, morphological	Aroclor 1254
reduced saccharin consumption and reduced saccharin preference ratio in the saccharin preference test in female rats exposed to PCB 77 or PCB 126		PCB 77 PCB 126

Mixture		Rat	Wistar	Oral-diet
Mixture		Rat	Long-Evans	Oral-gavage
Mixture		Rat	Long-Evans	Injection-ip
Congener		Rat	Sprague-Dawley	oral-diet
Mixture		rat	Long-Evans	Oral-gavage
Mixture		rat	Sprague-Dawley	Injection-ip
Mixture		Rat	Long-Evans	Oral-gavage
Mixture		Rat	Sprague Dawley	Oral-cookie
Mixture		Rat	Wistar	Oral-gavage
Congener		Rat	Sprague Dawley	Oral-gavage

Secondary				-60
Secondary				6
Secondary				7
Secondary				7
Secondary				6
Secondary				16
Primary		20		
Secondary				1
Secondary				10
Secondary				10



43			3	32
43			2	6
13			2	2.5
43				6
43			2	6
18			2	0.1
			2	10
45			2	15
16			2	25
16				0.086142322

32				
6				
2.5				
6				
10				
30				
15				
25				


all behavioral tasks were only performed in male pups. Examined max of 2 individuals per litter. Behaviors were monitored at PND 120 and PND 180. Reported PCB tissue levels in liver and brain.	Medium
provides AR1254 Lot #	Medium
MOA, rescued effects with T4	
auditory function assessed at 18 months of age	
dosing was only 5 days/wk for 4 wks	
doses were delivered using teddy graham cookies	

Seo et al. 1995	1995	197869		yes	Evaluated only PCB mixtures with < 4 congeners
Haake et al. 1987	1987	198618		yes	No neurological outcome data
Lilienthal et al. 1990	1990	198619	2173281	no	N/A
Levin et al. 1988	1988	198621		no	N/A
Linder et al. 1974	1974	198624		no	N/A
Wren et al.	1987	198626	2924471	yes	No neurological outcome data
Wren et al. 1987	1987	198627		yes	Exposure design deficiencies

open field testing brain weight operant conditioning active avoidance learning	Activity level/motor function Brain-histological, structural, morphological Cognitive-behavioral tests Emotional state	Clophen A30
delayed spatial alteration (spatial learning and memory)	Cognitive-behavioral tests	Aroclor 1016 Aroclor 1248
brain weight and histopathology	Brain-histological, structural, morphological	Aroclor 1254 Aroclor 1260
		Aroclor 1254
qualitative descriptions of brain lesions at necropsy	Brain-histological, structural, morphological	Aroclor 1254

Congener				
Mixture		Rat	Wistar	Oral-diet
Mixture		Rhesus monkey	Macaca Mulatta	Oral-diet
Mixture		Rat	Sherman	Oral-diet
mixture		Mink	Not reported	Oral-diet
Mixture		Mink	Mustela vison	Oral-diet

Secondary				-60
Secondary				Aroclor 1016: - 213 Aroclor 1248 (13 mo post- exposure): -943 Aroclor 1248 (32 mo post- exposure): -1521
Primary		184		



				0.43071161
				0.052352941
43			3	5
Aroclor 1016: (4 mo of age) Aroclor 1248 (13 mo post- exposure): -395 Aroclor 1248 (32 mo post- exposure): -973			2	0.00758 0.09 0.08
			2	7.2 1.5 6.9 1.5
			3	1

30				
0.0297 0.09 0.08				
37 7.6 35.4 7.4				
1				

<p>Aroclor 1016: Study doses reported as 0.00758 and 0.0297 mg/kg-d (HERO ID 199761, p 247)</p> <p>Aroclor 1248: Author estimated dose administered as 0.09 mg/kg-day (reported in HERO ID #199761) and Author estimated dose administered as 0.08 mg/kg-day (reported in HERO ID #199761)</p>

all behavioral tasks were only performed in male pups. Examined max of 2 individuals per litter? Behaviors were monitored at both PND 22 and PND 120. Contains PCB tissue levels in liver and brain.	
examined >1 AR mixture. Includes subsequent births from the same dam (multi-generational)	Aroclor 1016: Uninformative (critically deficient animal allocation) Aroclor 1248: Uninformative (critically deficient exposure method)
performed LD50 experiments with both diet and IV injections. Then performed 2 generation reproductive assays. No neurological data presented. Brain weights were measured, but not reported.	
Kit growth and survival, cause of death, testicular development, and liver size were measured. Male mating behavior was evaluated, but not enough information was provided to consider this an assay of social behavior.	
PCB brain tissue levels-ADME brain lesions at necropsy evaluated but not reported for animals exposed only to PCBs	

Schantz, SL, Moshtaghian, J, Ness, DK	1995	198638		yes	Evaluated only PCB mixtures with < 4 congeners
Arnold et al. 1993	1993	198642		yes	No neurological outcome data
Schantz, SL, Seo, BW, Moshtaghian, J, et al.	1996	198781		yes	Evaluated only PCB mixtures with < 4 congeners
Mayes et al. 1998	1998	198857		yes	No neurological outcome data
Pantaleoni et al. 1988	1988	198866	2206865	no	N/A

<p>∅ in delayed alternation (T-maze) in males (small ↓ in latency to start alternating for males) ; ↓ delayed alternation in females exposed to high dose PCB 28, 118, or 153 during the first or second block session periods but ∅ in the third block session.</p> <p>∅ working/reference memory errors in the radial arm maze; ↓ latency (seconds/arm entry) in male rats exposed to high dose PCB 153 but ∅ effect on latency for males exposed to other PCBs or in females</p>		<p>PCB 28 PCB 118 PCB 153</p>
<p>↓ working memory errors in the radial arm maze in both the low and high dose PCB 77 or PCB 126 groups</p> <p>∅ effect on delayed alternation in the T-maze in PCB-treated rats</p>		<p>PCB 77 PCB 126</p>
		<p>Aroclor 1016 Aroclor 1242 Aroclor 1254 Aroclor 1260</p>
<p>reflex development (surface righting, cliff avoidance, negative geotaxis), open field activity, swimming active avoidance</p>	<p>Activity level/motor function Emotional state</p>	<p>Fenclo 42</p>

Congener		Rat	Sprague Dawley	Oral-gavage
Congener		Rat	Sprague Dawley	Oral-gavage
Mixture				
Mixture		Rat	Fischer 344	Injection-ip Oral-gavage

Secondary				10
Secondary				10
Secondary				



16				0.27
				0.0075
16				6
			2	5 2 1

10 4 2				



brain weight and histopathology, optic and sciatic nerve histopathology, and spinal cord histopathology were evaluated, but the results were not reported	

Rice 1999	1999	198913		yes	Review
Rice, DC	1999	198915		yes	Evaluated only PCB mixtures with < 4 congeners
Cocchi, D, Tulipano, G, Colciago, A, et al.	2009	199561		yes	No neurological outcome data

		Breast milk mixture: PCBs 52, 66, 74, 105, 118, 138, 153, 156, 157, 180, 183, 187, 189, 194, 203
<p>↓ in T4 in 21 and 60 day old pups exposed to 0.25 or 1 ug/kg PCB 126 (larger difference at 21 days old);</p> <p>Ø delayed alternation performance using operant conditioning paradigm</p>		PCB 126
<p>Ø on free T3, T4, or T3/T4 ratio at PND 21 or 60</p> <p><b>variable</b> effects on somatostatin expression and growth hormone content in the brain, depending on brain region and sex of the animals</p>		Mixture: PCBs 126, 138, 153, 180

Mixture		Cynomolgus monkey	Macaca Fasicularis	Oral-syringe
Congener		Rat	Long-Evans	oral-diet (corn pop)
Mixture		Rat	Sprague Dawley	subcutaneous injection

Primary				
Secondary				-35
Secondary		~27		15



	168	308	2	0.0075
43				1
43				0.0075




Hany, J, Lilienthal, H, Roth-Härer, A, et al.	1999	199575		yes	Evaluated only PCB mixtures with < 4 congeners
Casey et al. 1999	1999	199578		no	N/A
Arnold et al. 1997	1997	199648	2199097	no	N/A
Crofton et al. 2000	2000	199653		no	N/A
Anon 2006	2006	199665	2200544	yes	Evaluated only PCB mixtures with < 4 congeners

<p>E1 group: locomotor activity in open field (PND 70), 1.5 mg/kg PCB 77 ↓ in outer zone during last two third of test session (Ø on total distance or in PCB 47 alone or PCB 77/47 co-treat groups); passive avoidance task (PND 85), ↓step-down latency in PCB 77 or PCB 47/77 co-treat group 5 min after conditioning (Ø at 4 or 24 h post-conditioning)</p> <p>E2 group: locomotor activity in open field: at PND 18, 0.5 mg/kg PCB 77 ↓ in outer zone during first third of test session; Ø on total distance at PND 18 or PND 80; on PND 340, ↑ distance and rearing behavior in all PCB-treated animals; variable effects on haloperidol-induced catalepsy</p>		<p>PCB 47 PCB 77</p>
<p>open field behavior (rearing ambulation) emotionality</p>	<p>Activity level/motor function Emotional state</p>	<p>Aroclor 1242</p>
<p>peripheral nerve histopathology, brain weight and histopathology</p>	<p>Brain-histological, structural, morphological</p>	<p>Aroclor 1254</p>
<p>auditory thresholds via reflex modification audiometry (PND 92-110), histological examination of cochlea</p>	<p>Sensory function</p>	<p>Aroclor 1254</p>

Congener		Rat	Long-Evans	subcutaneous injection
Mixture		Rat	Sprague Dawley	Inhalation Oral-diet
Mixture		Rhesus monkey	Macaca Mulatta	Oral-capsule
Mixture		Rat	Long-Evans	Oral-gavage
Congener				

Secondary				7
Primary		30		
Primary				
Secondary				6



18				0.006
			2	0.00046 0.0328
			2	0.005
43			2	8

0.00046 0.0328				
0.08				
8				

Doses presented in Table 1 (0.46 ug/kg-d) Doses presented in Table 1 (32.8 ug/kg-d)

used whole body inhalation. Compares inhalation and dietary exposure, ADME, also examines TH levels.	Low - high risk of bias Medium
Contains ADME data for infants and moms	
MOA ototoxicity	

Wang, XQ, Fang, J, Nunez, AA, et al.	2002	199666		yes	Evaluated only PCB mixtures with < 4 congeners
Lein et al. 2007	2007	199672		yes	No neurological outcome data
Bushnell, PJ and Rice, DC 1999 (see also 2155976 for erratum)	1999	199673		yes	Evaluated only PCB mixtures with < 4 congeners
Bushnell et al. 2002	2002	199676		no	N/A

<p>female sexual behavior: all PCB 77 and high (20mg/kg)  PCB 47 females ↓ lordosis quotient (sexual receptivity); PCB 77 females ↓ approach latency (Ø PCB 47); Ø effect of PCB 47 or 77 on other endpoints for female sexual behavior  male sexual behavior: Ø effect of PCB 47 or 77</p>		<p>PCB 47  PCB 77</p>
<p>Dendritic growth was assessed using Golgi analyses of CA1 hippocampal pyramidal neurons and cerebellar Purkinje cells. Also analyzed expression of spinophilin and RC3/neurogranin mRNA in the hippocampus, cerebellum, cortex and cortex</p>	<p>Brain-histological, structural, morphological</p>	<p>Aroclor 1254</p>
<p>a cued target-detection task, modeled after Posner's covert orienting method for humans, was used to assess visuospatial attention and a sustained attention test by means of a signal detection method; also did a challenge with CDP before doing above tests</p>		<p>PCB 126</p>
<p>functional observational battery, locomotor activity, habituation of motor activity  acquisition of visual discrimination  performance of a visual signal detection task</p>	<p>Activity level/motor function  Cognitive-behavioral tests  Emotional state  Sensory function</p>	<p>Aroclor 1254</p>

Congener		Rat	Long-Evans	subcutaneous injection
Mixture		Rat	Long-Evans	Oral-gavage
Congener		Rat	Long-Evans	Oral-diet
Mixture		Rat	Long-Evans	Oral-gavage

Secondary				7
Secondary				6
Secondary				-49
Secondary				6



18				5
43			2	6
43				3.2
43			2	1

6				
6				


assessed endpoints in male pups	
suggests suggest that PCB 126 may alter GABA-mediated pathways in the CNS during development; erratum published (HERO ID 2155976)	

Overmann et al. 1987	1987	199680		no	N/A
Rice et al. 1998	1998	199689	2195916	no	N/A
Crofton et al. 2000	2000	199692		no	N/A
Stewart et al. 2000	2000	199693		yes	Exposure design deficiencies
Sager, DB; Girard, DM	1994	199695		yes	No neurological outcome data
Kaya et al. 2002	2002	199715		no	N/A
Kuriyama, SN, Chahoud, I	2004	199724		yes	Evaluated only PCB mixtures with < 4 congeners

negative geotaxis, air righting electroshock seizure phases duration, brain weight auditory startle	Activity level/motor function Brain-histological, structural, morphological Sensory function	Aroclor 1254
3 spatial discrimination reversal tasks, differential reinforcement of low rate (DRL) 30-s schedule initiation reversal tasks	Cognitive-behavioral tests	Breast milk mixture: PCBs 52, 66, 74, 105, 118, 138, 153, 156, 157, 180, 183, 187, 189, 194, 203
auditory assessment and cochlear histological evaluation	Sensory function	Aroclor 1254
~ persistence of progressive-ratio reinforcement schedules.		
		Aroclor 1254
brain weight conditioned place preference sweet preference	Brain-histological, structural, morphological Sexual behavior Social behavior	Breast milk mixture: PCBs 28, 77, 101, 105, 118, 126, 138, 146, 153, 156, 169, 170, 180, 187
reflex development: ↑delay in cliff-drop aversion and ↓ latency for rotating rod reflex development in female offspring (∅ in reflexes in males) locomotor activity: ↑ activity (total movements and duration) in all offspring at PND 70-74 (∅ PND 30-34)		PCB 118

Mixture		Rat	Wistar	Oral-diet
Mixture		Cynomolgus monkey	Macaca Fasicularis	Oral-syringe
Mixture		Rat	Long-Evans	Oral-gavage
		rat	Sprague- Dawley	Oral-diet
Mixture				
Mixture		Rat	Long-Evans	Oral-diet
Congener		Rat	Sprague Dawley	oral-gavage

Secondary				0
Primary, pre-weaning				
Secondary				
Primary		20-65		
Secondary				
Secondary				6



43			2	0.27
	168	308	2	0.0075
			2	6
				86.1
			3	5
6				86.1

18.5				
0.0075				
6				
40				

Based on food intake and body weights as reported by the study, average daily doses were 0.27, 2.6, and 18.5 mg/kg-d, respectively.

	Medium
sensory effects	
Evaluated mating frequency, but not enough information was provided to consider this an assay of social behavior.	

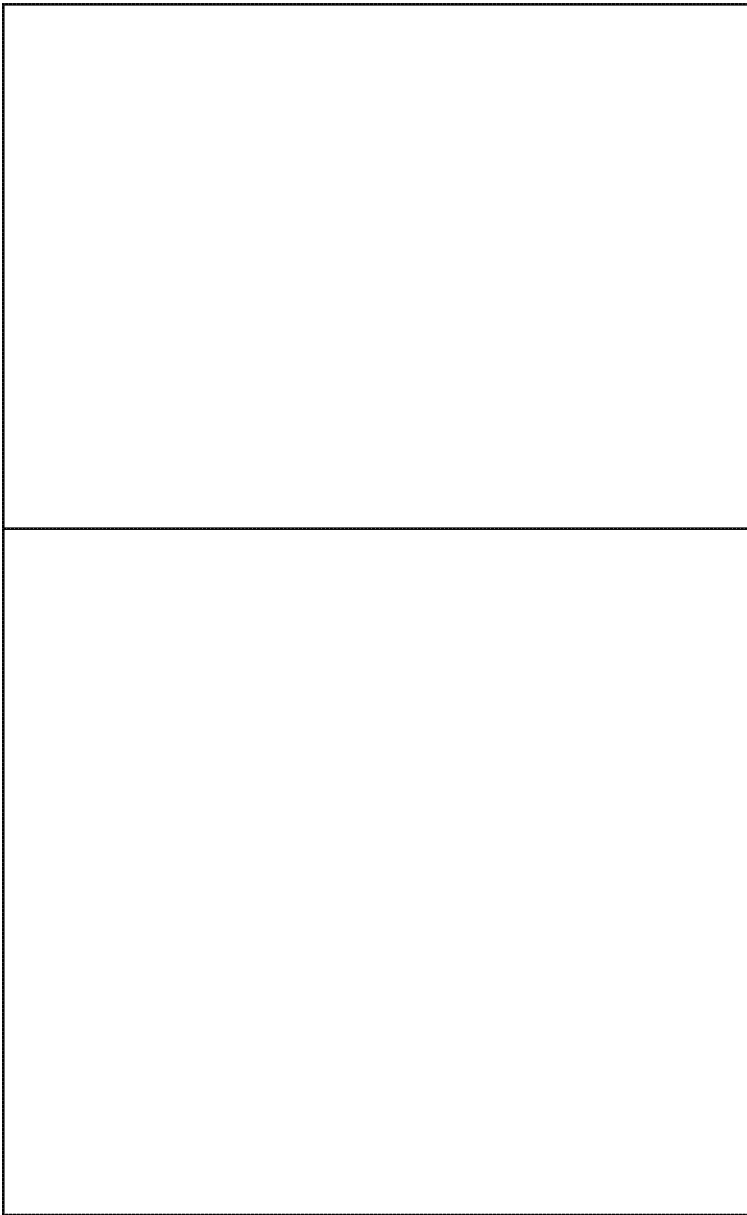
Donahue et al. 2004	2004	199740		yes	Evaluated only PCB mixtures with < 4 congeners
Eriksson, P, Fredriksson, A	1998	199742		yes	Evaluated only PCB mixtures with < 4 congeners

<p>all doses of PCB depressed ChAT activity in hippocampus with no significant alteration in the basal forebrain. In PCB-treated animals, short-term memory showed a trend toward improvement and long-term memory toward depression, but these trends were not significant</p>		<p>Mixture: PCBs 47, 77</p>
<p>spontaneous locomotor activity (open field test): variable effects at 2 and 4 months old spatial learning and memory (MWM): Ø effect at 5 months old receptor expression and biogenic amine levels (6 months old): ↓ density of nicotinic receptors in the hippocampus in 0.46 mg/kg PCB 126 animals; Ø effect on dopamine, DOPAC, HVA, 5-HT, and 5-HIAA levels in the striatum</p>		<p>PCB 105 PCB 126</p>

Congener		Rat	Sprague Dawley	oral-diet (dams)
Congener		mice	NMRI	oral-gavage




				0.130882353
				0.098623853


Schantz et al. 1989	1989	199761		no	N/A
Powers et al. 2009	2009	199798		no	N/A
Rice et al. 1997	1997	199799		no	N/A

two choice discrimination reversal learning (spatial, color, and shape)	Cognitive-behavioral tests	Aroclor 1016 Aroclor 1248
brain weight auditory function assessed at PND 200 distortion product otoacoustic emissions (DPOAEs) and auditory brainstem responses (ABRs)	Brain-histological, structural, morphological Sensory function	Fox River PCB mixture
multiple fixed interval (FI) fixed ratio, interresponse times	Cognitive-behavioral tests	Breast milk mixture: PCBs 52, 66, 74, 105, 118, 138, 153, 156, 157, 180, 183, 187, 189, 194, 203

Mixture		Rhesus monkey	Macaca Mulatta	Oral-diet
Mixture		Rat	Long-Evans	Oral-cookie
Mixture		Cynomolgus monkey	Macaca Fasicularis	Oral-syringe

Secondary				<p>Aroclor 1016: - 213</p> <p>Aroclor 1248 (13 mo post- exposure): -943</p> <p>Aroclor 1248 (concurrent exposure): -487</p> <p>Aroclor 1248 (32 mo post- exposure): -1521</p>
Secondary				-28
Primary, pre-weaning				



Aroclor 1016: (4 mo of age) Aroclor 1248 (13 mo post- exposure): -395 Aroclor 1248 (concurrent exposure): (4 mo of age) Aroclor 1248 (32 mo post- exposure): -973			2	0.00758 0.09 0.01 0.08
43			2	1
	168	308	2	0.0075

0.0297 0.09 0.01 0.08				
3				
0.0075				

Study doses reported as 0.00758 and 0.0297 mg/kg-d (p 247)

Study dose reported as 0.09 mg/kg-d (p 245)

Study dose reported as 0.03 mg/kg-d (3 d/wk) (p 245)

Study dose reported as 0.08 mg/kg-d (p 246)

	<p>Critically Deficient. Based on information reported by Barsotti and van Miller (1984; 199568), the Aroclor 1016-exposed animals were acquired separately from the control animals, and the evidence presented to dismiss any potential differences between these groups does not eliminate the potential for evaluations of neurological impacts in offspring to be biased as a result of using exposed and control groups of animals that were also of different ages and kept in captivity for different lengths of time.</p> <p>Critically Deficient. Toxicokinetic data reported by Allen et al. 1980 (201752), Bowman et al. 1981 (199846), and Schantz et al. 1989 (199761) demonstrate that there was little-to-no difference in PCB body burdens between the control and exposed groups in either dams at the time of pregnancy and lactation or offspring at any time during the experiment for groups conceived a year or more after the end of the exposure period.</p>
includes brain/serum levels of PCBs-ADME	Same cohort as 199689

Bowman et al. 1981	1981	199846		no	N/A
Rice et al. 1997	1997	199848		no	N/A
Lilienthal, H, Fastabend, A, Hany, J, et al.	2000	199855		yes	No neurological outcome data
Rice and Hayward 1998	1998	199868	2190249	yes	Evaluated only PCB mixtures with < 4 congeners
Rice et al. 1999	1999	199869		no	N/A
Rice, DC, Hayward, S	1999	199870		yes	Evaluated only PCB mixtures with < 4 congeners
Roegge et al. 2000	2000	199872		no	N/A
Roegge et al. 2006	2006	199873		no	N/A
Eriksson 1988	1988	201423		yes	No neurological outcome data

locomotor activity	Activity level/motor function	Aroclor 1248
nonspatial discrimination reversal problems, spatial delayed alternation task	Cognitive-behavioral tests	Breast milk mixture: PCBs 52, 66, 74, 105, 118, 138, 153, 156, 157, 180, 183, 187, 189, 194, 203
no significant effects on behavior		PCB 126
relative reinforcement schedule and progressive ratio schedule	Cognitive-behavioral tests	Breast milk mixture: PCBs 52, 66, 74, 105, 118, 138, 153, 156, 157, 180, 183, 187, 189, 194, 203
variable effects on operant conditioning (depending on reinforcement schedule)		PCB 126
spatial learning and memory using the radial arm maze	Cognitive-behavioral tests	Aroclor 1254
cerebellar histopathology	Brain-histological, structural, morphological	Aroclor 1254

Mixture		Rhesus monkey	Macaca Mulatta	Oral-diet
Mixture		Cynomolgus monkey	Macaca Fasicularis	Oral-syringe
Congener		rat	Long Evans	oral
Mixture		Cynomolgus monkey	Macaca Fasicularis	Oral-syringe
Congener		rats	Long-Evans	oral-diet (corn pop)
Mixture		Rat	Long-Evans	Oral-gavage
Mixture		Rat	Long-Evans	Oral-cookie

Secondary				Aroclor 1248 (concurrent exposure): -487 Aroclor 1248 (10.5 mo post-exposure): -867 Aroclor 1248 (concurrent exposure): -548
Primary, pre-weaning				
Secondary				-35
Primary, pre-weaning				
Secondary				-35
Secondary				6
Secondary				-28



Aroclor 1248 (concurrent exposure): (3 mo of age) Aroclor 1248 (10.5 mo post- exposure): -319 Aroclor 1248 (concurrent exposure): (4 mo of age)			2	0.09 0.006
	168	308	2	0.0075
				20
43				20
	168	308	2	0.0075
43				0.344569288
43			2	6
38			2	6
				2.650095602

0.09 0.01				
0.0075				
0.0075				
6				
6				

Average study dose calculated from data provided in  
Table 1  
Average study dose calculated from data provided in  
Table 2  
Average study doses calculated from data provided in  
Table 3

includes brain/serum levels of PCBs-ADME	Same cohort as 199689
discusses thyroxin, but no mention of measurement in materials and methods or results	
	Same cohort as 199689

Eriksson, P, Fredriksson, A	1996	201424		yes	Evaluated only PCB mixtures with < 4 congeners
Eriksson, P, Fredriksson, A	1996	201425		yes	Evaluated only PCB mixtures with < 4 congeners
Eriksson et al. 1991	1991	201426	2161089	yes	Evaluated only PCB mixtures with < 4 congeners

<p>spontaneous locomotor activity (open field test): variable effects of PCB 28 and PCB 52, Ø effect of PCB 188 and PCB 156</p> <p>spatial learning and memory (MWM): Ø effect of PCB 118, 156, 28; ↑ latency to reach platform in PCB 52 animals during reversal learning phase</p> <p>radial arm maze: Ø effect of PCB 118, 156, 28; ↑ latency and ↑ errors in PCB 52 animals</p> <p>receptor expression and biogenic amine levels: ↑ proportion of high-affinity nicotinic receptors in PCB 52-treated animals in the cerebral cortex (Ø effect in PCB 28 animals); Ø effect on muscarinic receptor density in cerebral cortex in any treatment group; Ø effect on dopamine, DOPAC, HVA, 5-HT, and 5-HIAA levels in the striatum</p>		<p>PCB 28 PCB 52 PCB 118 PCB 156</p>
<p>spontaneous locomotor activity: variable effects of PCB 52 in 4 month old animals; ↓ activity in PCB-treated animals compared to controls after nicotine treatment; Ø difference between PCB-treated and controls following amphetamine exposure</p>		<p>PCB 52</p>
<p>Locomotor activity at 4 months of age; muscarinic receptor density and binding activity in different brain regions</p>		<p>PCB 77</p>

Congener		mice	NMRI	oral-gavage
Congener		mice	NMRI	oral-gavage
Congener		Mouse	NMRI	Oral-gavage

Primary		1		



				5
				1
				0.107677903



also assess effect of nicotine or amphetamine co-exposure on locomotor activity	

Holene, E, Nafstad, I, Skaare, JU, et al.	1995	201438	2166595	yes	Evaluated only PCB mixtures with < 4 congeners
Juarez de Ku et al. 1994	1994	201453	2159458	yes	No neurological outcome data
Morse et al. 1996	1996	201472		no	N/A
Rosin and Martin 1981	1981	201490		no	N/A
Schantz, SL, Seo, BW, Wong, PW, et al.	1997	201498		yes	Evaluated only PCB mixtures with < 4 congeners
Seegal et al. 1986	1986	201511		no	N/A

<p>reflex development: Ø in reflex development between controls and PCB-treated</p> <p>operant conditioning: ↓ visual discrimination learning (↑ perseveration and ↑ unnecessary tray visits) in PCB 126 group and PCB 118 high dose groups and ↑ activity (↑ lever presses) in all PCB-treated groups</p>		<p>PCB 118</p> <p>PCB 126</p>
		Aroclor 1254
<p>levels of serotonin (5-HT) and serotonin metabolites (HIAA) in the brain and olfactory tract</p>	Neurotransmitter levels	Aroclor 1254
Spontaneous motor activity	Activity level/motor function	Aroclor 1254
<p>locomotor activity (open field): ↓ activity in open field as adults</p> <p>radial arm maze (working memory): variable effect on number of errors</p> <p>delayed spatial alternation (T-maze): ↓ latency in PCB 77 treated animals; Ø effect in PCB 47 animals</p> <p>Haloperidol-induced catalepsy: effects (depending on brain region and PCB 95 dose level)</p>		PCB 95
<p>serotonin (5-HT) and serotonin metabolite levels (5-HIAA) in various brain regions (frontal cortex, hippocampus, hypothalamus, and lateral olfactory bulb)</p>	Neurotransmitter levels	<p>Aroclor 1016</p> <p>Aroclor 1260</p>

Congener		rat	albino Lewis	oral-gavage
Mixture		Rat	Sprague Dawley	Oral-diet
Mixture		Rat	Wistar	Oral-gavage
Mixture		Mouse	CD1	Oral-gavage
Congener		rat	Sprague Dawley	oral-gavage (corn pop)
Mixture		rat	Wistar	Oral-gavage

Secondary				10
Secondary		36		0
Secondary				10
Primary		1 14		
Secondary				10
Primary		1		



20				3.2
37			3	62.5
16			2	5
			2	
16				0.43071161
			2	500

250				
25				
1000				

30, 100 or 500 (varied by expt)

evaluated choline acetyltransferase in hippocampus, basal forebrain, and cerebral cortex, but not neurotransmitter levels	

Seegal et al. 1991	1991	201512		no	N/A
Seegal et al. 1994	1994	201513		no	N/A
Weinand-Härer, A, Lilienthal, H, Bucholski, KA, et al.	1997	201526		yes	Evaluated only PCB mixtures with < 4 congeners
Zoeller et al. 2000	2000	201532		yes	No neurological outcome data
Abrahamson and Allen 1973	1973	201746		no	N/A
Agrawal et al. 1981	1981	201747		yes	Evaluated only PCB mixtures with < 4 congeners
Allen and Abrahamson 1973	1973	201750		no	N/A
Allen et al. 1973	1973	201751		yes	No neurological outcome data

concentrations of dopamine and its metabolites in the caudate, putamen, substantia nigra, and hypothalamus	Neurotransmitter levels	Aroclor 1016 Aroclor 1260
concentrations of dopamine in the caudate nucleus, putamen and substantia nigra	Neurotransmitter levels	Aroclor 1016 Aroclor 1260
locomotor activity (open field): ↑ activity in last third of test session in PCB 77 animals radial arm maze (working memory): Ø effect passive avoidance: Ø effect haloperidol-induced catalepsy: ↑latency in PCB 77 animals		PCB 47 PCB 77
observed reduced T4 in pups following gestational exposure, as well as altered RC3/Neuogranin and myelin basic protein expression patterns in the brain.	Brain-histological, structural, morphological	Aroclor 1254
brain weight	Brain-histological, structural, morphological	Aroclor 1248
↑ Spontaneous motor activity ("spinner" phenotype) ↓ Dopamine levels ↓ Dopamine receptor binding in corpus striatum		PCB 77
brain weight	Brain-histological, structural, morphological	Aroclor 1248 Aroclor 1254 Aroclor 1262

Mixture		Pigtail monkey	Macaca Nemestrina	Oral-cookie
Mixture		Pigtail monkey	Macaca Nemestrina	Oral-cookie
Congener		rat	Wistar	subcutaneous injection
Mixture		Rat	Sprague Dawley	Oral-diet
Mixture		Rhesus monkey	Macaca Mulatta	Oral-gavage
Congener		Mouse	CD-1	Oral-gavage
Mixture		Rat	Sprague Dawley	Oral-diet

Primary		140		
Primary		140		
Secondary				7
Secondary				6
Primary, pre-weaning				
Secondary				10
Primary		42		



			2	0.8
			2	3.2
18				25
43			3	1
	198	228	2	35
16				10
			3	
				1

3.2				
3.2				
8				
35				

0.1% (convert to mg/kg)

ADME- also includes brain measurements by congeners	
This may be the same animals in 202763	
haloperidol-induced catalepsy	
dosed with a cookie	
Evaluated offspring at PND 4 and 21 for "spinner" (hyperactivity) phenotype. Evaluated spontaneous motor activity and dopamine levels/receptor binding in the corpus striatum at 1 year of age in controls, "spinners", and "non-spinners".	
dose administered needs some extrapolation	

Allen et al. 1979	1979	201753		yes	No neurological outcome data
Allen, JR, Carstens, LA, Barsotti, DA	1974	201754		yes	No neurological outcome data
Altmann et al. 1995	1995	201757		yes	Evaluated only PCB mixtures with < 4 congeners
Aulerich et al. 1985	1985	201773	2152680	no	N/A
Aulerich et al. 1987	1987	201774		yes	Evaluated only PCB mixtures with < 4 congeners
Biocca et al. 1981	1981	201793		yes	No neurological outcome data
Bowman and Heironimus 1981	1981	201796	2201021	no	N/A

menstrual cycling, abortions, resorptions, still births, infant body weight; qualitative data on learning and hyperactivity; references companion publication from 1978		Aroclor 1248
	Brain-histological, structural, morphological	
electrophysiology: long term potentiation (LTP) was measured in visual cortex and hippocampus in male rat pups		PCB 77
brain weight neurotransmitter levels in various brain regions	Brain-histological, structural, morphological Neurotransmitter levels	Aroclor 1254
brain weight		PCB 169
Body weight, mortality, organ weights, hematological findings (leukocytes, lymphocytes, neutrophils, serum proteins, globulins), pathology of liver/thymus/spleen/heart, Tissue PCB levels were recorded in feed, adipose, and liver		PCB 136 PCB 153 PCB 155 PCB 169
locomotor activity, post exposure activity	Activity level/motor function	Aroclor 1248

		Monkey	Macaca Mulatta	Oral-diet
Congener		Rat	Wistar	SC injection
Mixture		mink	standard dark	Oral-diet
Congener		MInk	pastel	Oral-diet
Congener		Mouse	C57BL6	Oral-diet
Mixture		Rhesus monkey	Macaca Mulatta	Oral-diet

Secondary		210		
Secondary				7
Primary				
Primary		135		
Primary		28		
Secondary				-487



				1.9
				3
18				1
			3	2.5
				6
				3
<i>(3 mo of age)</i>			2	0.09

2.5				
0.09				



neurological data presented qualitatively but not focus of paper. Also examined TCDD and PBBs in the same study.	
only maternal brain weight is reported	
measured in male rats	
also evaluated reproductive, endocrine, hepatic, metabolic (body weight), endpoints	
All animals at highest dose (300ppm) died.	
<p>testing took place 44 months after exposure- I believe these are the same organisms studied in another Bowman report, but with the testing repeated at an older age.</p> <p>Duplicate entry said "other information is reported in sister reports. Authors hypothesize that measured behavior 4 years after initial PCB exposure and after clearance of measurable PCB residues from mesenteric fat demonstrate that developmental changes are enduring and irreversible"</p>	

Bowman et al. 1978	1978	201797		no	N/A
Bruckner et al. 1973	1973	201809	2155498	no	N/A
Chou et al. 1979	1979	202192		yes	Evaluated only PCB mixtures with < 4 congeners

<p>locomotor activity test</p> <p>WGTA discrimination tests and general procedure spatial reversals, color reversals, shape discrimination reversals, partial reinforcement, probability learning, progressive probability shift, object alternation learning, object alternation learning set</p>	<p>Activity level/motor function</p> <p>Cognitive-behavioral tests</p>	<p>Aroclor 1248</p>
<p>brain histopathology</p>	<p>Brain-histological, structural, morphological</p>	<p>Aroclor 1242</p>
<p>Motor "spinning" was observed in a subset of PCB treated animals. These "spinnners" were evaluated against control and non-spinning littermates, evaluating dopamine agonists/antagonists on spinning, and histopathology using light and confocal microscopy.</p>		<p>PCB 77</p>

Mixture		Rhesus monkey	Macaca Mulatta	Oral-diet
Mixture		Rat	Sprague- Dawley	Oral-gavage
Congener		Mouse	CD-1	oral-NR

Secondary				-487
Primary		1		
Secondary				10



<i>(3 mo of age)</i>			2	0.09
			2	4000
16				0.000001

0.09				
4000				

Average study dose calculated from data provided in  
Table 1 (HERO ID #199846)

<p>only animals from the 2.5ppm group survived for testing. Many tests were far removed from developmental exposure; Tests were correlated to PCB body burdens over time.</p>	
<p>method of oral dosing not specified. Largely qualitative/microscopy images- good for MOA; also examines musculature</p>	

Chu et al. 1998	1998	202193	2157756	yes	Evaluated only PCB mixtures with < 4 congeners
Chu, I, Villeneuve, DC, Yagminas, A, et al.	1995	202195		yes	Evaluated only PCB mixtures with < 4 congeners
Chu et al. 1994	1994	202196	2157746	yes	Evaluated only PCB mixtures with < 4 congeners

<p>dopamine in the caudate nucleus, homovanillic acid in caudate nucleus and nucleus accumbens (decreased). 5-hydroxytryptamine and 5-hydroxyindoleacetic acid increased in the substantia nigra region.</p> <p>(Duplicate entry said "biogenic amine levels in the brain: ↓ dopamine, HVA levels in caudate nucleus or nucleus accumbens; ↑ HIAA and 5-HT levels in the substantia nigra (all at highest PCB dose)")</p>		PCB 105
<p>biogenic amine levels in the brain: ↓ dopamine and HVA levels in caudate nucleus or substantia nigra of females at highest PCB 118 dose; ↑ in DOPAC in nucleus accumbens of male mice treated with highest dose of PCB 77</p>		PCB 77 PCB 118
<p>↑ brain weight (relative to body weight); Ø brain histopathology; Ø brain biogenic amine levels</p> <p>(Duplicate entry said "brain weight: ↑ in males and females in 100ppb treatment group biogenic amine levels in the brain: Ø effect ")</p>		PCB 126

Congener		Rat	Sprague Dawley	Oral-diet
Congener		rat	Sprague Dawley	oral-diet
Congener		rat	Sprague- Dawley	oral-diet

Primary		91		
Primary		90		
Primary		90		



				0.025
				6
				exclude species



includes tissue residue data, as well as many other liver, hematologic, and immune endpoints. Authors make an effort to approximate daily consumption and a NOAEL.	
An additional group of 10 male and 10 female animals was orally given a loading dose of 5 ug/kg of the PCB in com oil at the start of the study and was then placed on the 10 ppb PCB diet in the same fashion as the other animals	

An additional group of 10 male and 10 female animals was orally given a loading dose of 5 ug/kg of the PCB in com oil at the start of the study and was then placed on the 10 ppb PCB diet in the same fashion as the other animals

Chu, I, Villeneuve, DC, Yagminas, A, et al.	1996	202197		yes	Evaluated only PCB mixtures with < 4 congeners
Chu, I, Villeneuve, DC, Yagminas, A, et al.	1996	202198		yes	Evaluated only PCB mixtures with < 4 congeners
Crofton, KM, Rice, DC	1999	202212		yes	Evaluated only PCB mixtures with < 4 congeners
Freeman et al. 2000	2000	202272		no	N/A
Gray et al. 1993	1993	202290	2200772	yes	No neurological outcome data
Hansen, LG; Byerly, CS; Metcalf, RL; Bevill, RF	1975	202309		no	N/A
Hansen, LG; Wilson, DW; Byerly, CS	1976	202313	2165171	no	N/A
Hany et al. 1999	1999	202314		no	N/A
Herr et al. 1996	1996	202323	2205110	no	N/A

biogenic amine levels in the brain: ↓ dopamine, 5-HT, DOPAC, and DOPAC/DA ratio in various brain regions of females exposed to ≥ 5 ppm PCB; ↑ 5HIAA/5HT ratio in 50 ppm PCB males		PCB 153
biogenic amine levels in the brain: Ø effect on males; ↓ dopamine in ≥ 0.5 ppm PCB-treated females		PCB 28
hearing loss: ↑ auditory thresholds in 1 ug/kg PCB 126 animals at low frequency tones		PCB 126
functional observational battery and motor activity assessment histopathological analysis of brain tissues	Activity level/motor function Brain-histological, structural, morphological	Aroclor 1016 Aroclor 1242 Aroclor 1254 Aroclor 1260
focus of paper is endocrine and reproductive effects; pituitary weight was measured		Aroclor 1254
relative brain weight, brain gross pathology and histopathology	Brain-histological, structural, morphological	Aroclor 1242
brain weight	Brain-histological, structural, morphological	Aroclor 1242 Aroclor 1254
brain weight sex-specific behavior	Brain-histological, structural, morphological Sexual behavior	Aroclor 1254 Breast milk mixture: PCBs 28, 77, 101, 105, 118, 126, 138, 146, 153, 156, 169, 170, 180, 187
brainstem auditory evoked responses, cochlear and auditory function	Sensory function	Aroclor 1254

Congener		rat	Sprague Dawley	oral-diet
Congener		rat	Sprague Dawley	oral-diet
Congener		rat	Long Evans	oral-diet (corn pop)
Mixture		Rat	Sprague- Dawley	Oral-diet
		Rat	Fischer 344	oral-gavage
Mixture		Swine	mixed breed	Oral-diet
Mixture		Sheep Swine		Oral-diet
Mixture		Rat	Long-Evans	Oral-diet
Mixture		Rat	Long-Evans	Oral-gavage

Primary		90		
Primary		90		
Secondary				-49
Primary		365		
Primary		35-150		
Secondary				
Primary		105 91		
Secondary				
Secondary				6



				0.098623853
				18
43				5
			3	50 25
				1
			3	20
			3	20
22			3	40
43			2	1

200 100				
20				
20				
40				
8				


ADME data includes PCB residues in the brain	
focus of study on growth and GI lesions	
same animals from Goldey 1995b; brainstem auditory evoked responses assessed at about 1 year old	

Holene, E, Nafstad, I, Skaare, JU, et al.	1998	202325		yes	Evaluated only PCB mixtures with < 4 congeners
Hornshaw et al. 1986	1986	202328		no	N/A
Iatropoulos et al. 1978	1978	202339		no	N/A
Kihlström et al.	1992	202369		no	N/A
Kimura and Baba 1973	1973	202375		yes	No neurological outcome data
Koller et al. 1977	1977	202385		yes	No neurological outcome data
Lecavalier, P, Chu, I, Yagminas, A, et al.	1997	202407		yes	Evaluated only PCB mixtures with < 4 congeners
Morse et al. 1996	1996	202450		no	N/A
Morse, DC, Wehler, EK, Wesseling, W, et al.	1996	202452		yes	No neurological outcome data
Nishida et al. 1997	1997	202460		no	N/A
Provost et al. 1999	1999	202486		no	N/A
Rodriguez et al. 1997	1997	202493		yes	Evaluated only PCB mixtures with < 4 congeners
Seegal et al. 1986	1986	202527		no	N/A

reflex development: Ø effect operant conditioning: ↑ lever presses and unnecessary tray visits (activity) in PCB 126 and 153-treated animals; other variable effects		PCB 126 PCB 153
listlessness nervousness	Activity level Emotional state	
central nervous system histopathology	Brain-histological, structural, morphological	Clophen A30
brain weight	Brain-histological, structural, morphological	Aroclor 1254 Clophen A50
intracranial abscess observed in several treated rats but not controls		Kanechlor 400
dopamine levels: ↓ in 50 ppm females in frontal cortex and hippocampus		PCB 128
brain weight	Brain-histological, structural, morphological	Aroclor 1254
motor activity sweet preference using saccharin preference	Activity level/motor function Sexual behavior	Aroclor 1254
spatial learning in the Morris water maze	Cognitive-behavioral tests	Aroclor 1254
concentrations of dopamine (DA) and its major metabolites in caudate nucleus and lateral olfactory tract	Neurotransmitter levels	Aroclor 1016 Aroclor 1260

Congener		rat	DA/OLA/HS D	oral-gavage
Mixture		Rhesus monkey	Macaca Mulatta	Oral-gavage
mixture		Mink	Standard breed	Oral-diet
Mixture		rat	Donryu	Oral-diet
Congener		rat	Sprague Dawley	oral-diet
Mixture		Rat	Wistar	Oral-gavage
Mixture		Rat	Long-Evans	Oral-gavage
Mixture		Rat	Sprague Dawley	Oral-diet
Congener				
Mixture		rat	Wistar	Oral-gavage

				25
Primary	46	22		
Primary		400		
Primary		90		
Secondary				10
Primary	60	28		
Secondary				0
Primary		1		



35				5.383895131
				172.2846442
			2	16
			2	16.30098
				0.098623853
				0.137667304
16			2	5
				1
			2	7.1
52			3	1.25
				0.086142322
			2	500

16				
25				
71				
12.5				
1000				

Dosing start and end days are based on the monkey that was exposed for 22 d, beginning at age 46 d and ending at age 68 d
Average dose and body weight calculated from data presented in Table 1
After adjustment for continuous exposure, the doses were 7.1, 21, and 71 mg/kg-d

Cannot access full paper through pubmed or WoS	
no statistical analyses appear to have been performed	

Seegal et al. 1997	1997	202529		yes	Evaluated only PCB mixtures with < 4 congeners
Tilson, HA; Davis, GJ; McLachlan, JA; Lucier, GW	1979	202563		yes	Evaluated only PCB mixtures with < 4 congeners
Vos et al. 1972	1972	202581		yes	No neurological outcome data
Vox and Van Driel-Grootenhuys 1972	1972	202583	2192218	yes	No neurological outcome data
Ward 1985	1985	202585		no	N/A
Schuur et al. 1998	1998	202649		yes	No neurological outcome data
Villeneuve et al. 1971	1971	202651		no	N/A
Holene, E, Nafstad, I, Skaare, JU, et al.	1999	202662		yes	Evaluated only PCB mixtures with < 4 congeners

variable effects on dopamine, DOPAC, and HVA changes in the frontal cortex, substantia nigra, and caudate nucleus. In some cases, there was an age x dose interaction in responses.		PCB 47 PCB 77
reflex tests: eye-blink and ear-twitch reflexes, response to painful stimuli, orientation to olfactory and auditory stimuli, body posture on tilting platform spontaneous motor activity diurnal motor activity visual placement forelimb grip strength acquisition of avoidance behavior performance on the wire rod		PCB 77
		Aroclor 1260 Clophen A60
brain histopathology	Brain-histological, structural, morphological	Aroclor 1254
Measures SULT activity in brain tissues, largely TH study.		Aroclor 1254
brain weight	Brain-histological, structural, morphological	Aroclor 1254
reflex development: Ø effect operant conditioning: Ø/variable effects thyroid hormone levels: ↓ total T4 at PND 14 (but no effect at other time points); Ø effect on free T4 at any time point		PCB 153

Congener		rat	Sprague-Dawley	Oral-diet
Congener		mouse	CD-1	oral-gavage
		guinea pigs		
Mixture				
		Rat	Wistar	oral-NR
Mixture		Rabbit Rat		
Congener		rat	DA/OLA/HS D	oral-gavage

Secondary				6
Secondary				10
		42		
Secondary		8		
				25



43				0.00000001
16				6
				1.5
				1
				1 6.25
35				

10 100				


neurobehavioral tests were performed at 36 and 65 days of age; the experimental group comprised 8 TCB-spinners and 8 TCB-nonspinners; the spinners were exposed pups who were observed to display marked hyperactivity or rotational behavior prior to weaning (spinning syndrome)	
Measures SULT activity in brain tissues, largely TH study.	

Seegal et al. 1992	1992	202763		no	N/A
Brezner et al. 1984	1984	202791		no	N/A
Corey et al. 1996	1996	202841		no	N/A
Takahashi et al. 2009	2009	587230		yes	No neurological outcome data
Altmann et al. 2001	2001	594585	2151845	no	N/A
Ntp 2006	2006	595164		yes	Evaluated only PCB mixtures with < 4 congeners
Ntp	2006	595167		yes	Evaluated only PCB mixtures with < 4 congeners

regional brain dopamine concentrations	Neurotransmitter levels	Aroclor 1016 Aroclor 1260
sexual receptivity behavior maternal behavior	Sexual behavior Social behavior	Aroclor 1254
radial arm maze memory testing	Cognitive-behavioral tests	Aroclor 1254
4-OH-PCB106 affected mRNA expression of glutamate receptors as well as that of thyroid hormone-responsive genes in region-specific manners; 4-OH-PCB106 exposure increased mRNA expression of genes related to exocytosis in the three brain regions - cerebral cortex, the hippocampus, and the striatum		OH-PCB 106 OH-PCB 107
long term potentiation (LTP) in the visual cortex and hippocampus	Neurophysiology	Aroclor 1254 Breast milk mixture: PCBs 28, 77, 101, 105, 118, 126, 138, 146, 153, 156, 169, 170, 180, 187

Mixture		Pigtail monkey	Macaca Nemestrina	Oral-cookie
Mixture		rat	Wistar	Oral-gavage
Mixture		Rat	Sprague Dawley	Oral-diet
		rat	F344/N	subcutaneously implanted osmotic pump
Mixture		Rat	Long-Evans	Oral-diet
Congener				

Primary		140		
Primary	76	30		
Secondary				
Secondary		GD 7 until postnatal day (PND) 1		
Secondary				



			2	3.2
			2	10
			3	125
			3	5

3.2				
10				
250				
40				


ADME- also includes brain measurements by congeners	
ADME data included PCB residues in the brains of dams, fetuses, and pups	Maternal behavior: Low - high risk of bias
unique exposure set up- exposed during different windows of conception, weaning, and 60 days of age	
estimates of food intake data are provided. Recordings provided in females (hero ID XX reports male data)	

Kostyniak, PJ; Hansen, LG; Widholm, JJ; Fitzpatrick, RD; Olson, JR; Helferich, JL; Kim, KH; Sable, HJK; Seegal, RF; Pessah, IN; Schantz, SL	2005	595287		no	N/A
Seegal, RF; Brosch KO	2005	597455		yes	Evaluated only PCB mixtures with < 4 congeners
Dziennis et al. 2008	2008	604867		no	N/A
Venkataraman et al. 2008	2008	621853		yes	No neurological outcome data

brain weight	Brain-histological, structural, morphological	Mixture: Aroclors 1242, 1254, 1260
dopamine concentration in the prefrontal cortex		PCB 47 PCB 77 PCB 126
sensitivity to ischemic brain injury	Brain-histological, structural, morphological	Aroclor 1254
Found that PCB alters membrane bound ATPase's and cholinergic function by inducing oxidative stress in brain regions, which can be protected by melatonin		Aroclor 1254

Mixture				
Congener		rat	Sprague-Dawley	oral-diet
Mixture		rat	Wistar	Oral-diet
		rat	Wistar	IP injection

Secondary				6
Secondary				-14
Primary		30		



43				
43				0.1

1				


<p>test substances were diluted in corn oil and placed on vanilla wafer cookies; prefrontal cortical dopamine concentrations were measured when the offspring were 35, 60, or 90 days old; this publication also includes prepubertal uterine wet weight experiments that measured uterine wet weight and relative uterine weight in female Sprague-Dawley-derived rats on PND24 that were exposed to PCB 77, 126, 47, or 169 on PND21–22 by IP injection; in an additional experiment, animals were exposed to the PCB congeners along with the estrogen receptor antagonist ICI 182,780 on PND21–23</p>	
<p>When offspring reached 225–275 g body weight (6–8 weeks for males; 8–10 weeks for females), we induced transient focal cerebral ischemia</p>	

Sauer et al. 1994	1994	625019		yes	Evaluated only PCB mixtures with < 4 congeners
Colciago et al. 2009	2009	625490		no	N/A
French et al. 2001	2001	625514		yes	No neurological outcome data
Zahalka et al. 2001	2001	625812		no	N/A
Seegal et al. 2002	2002	625951		no	N/A
McLanahan et al. 2007	2007	626367		yes	Evaluated only PCB mixtures with < 4 congeners

<p>report small effects on reflexes and eye opening  ↓forelimb and hindlimb grip strength in adolescent animals  Ø in glucose uptake in the brain  ↑ dopamine levels in animals post-natally; increased deiodination of T3 and T4 thyroid hormones in the brains of fetal and neonatal animals</p>		<p>PCB 77  PCB 169</p>
<p>locomotor activity  Morris water maze (spatial memory)  passive avoidance, forced swimming test (depression),  elevated zero maze test (anxiety)  male and female sexual behavior</p>	<p>Activity level/motor function  Cognitive-behavioral tests  Emotional state  Sexual behavior</p>	<p>Mixture: PCBs 126, 138, 153, 180</p>
<p>weight of various brain regions  spatial learning and memory using t-maze delayed alternation and Morris water maze tasks  dopamine and norepinephrine levels in 6 brain regions</p>	<p>Brain-histological, structural, morphological  Cognitive-behavioral tests  Neurotransmitter levels</p>	<p>Aroclor 1016  Aroclor 1254</p>
<p>dopamine levels in dialysates (extra neuronal DA) from the striatum</p>	<p>Neurotransmitter levels</p>	<p>Aroclor 1254</p>

Congener		rat	NR?	oral-diet?
Mixture		Rat	Sprague Dawley	Injection-sc
Mixture		Rat	Long-Evans	Oral-gavage
Mixture		rat	Sprague- Dawley	Oral-diet
Congener				

		NR		
Secondary				15
Secondary				
Primary				



43			2	3.9
			2	10 8
			2	25

3.9				
10 8				
25				

Dose is duration-adjusted from 10 mg/kg-d based on daily dosing from GD15-19 and dosing twice a week from PND1-21 (11 total doses)

	Emotional state: Low Passive avoidance: Medium Morris water maze: Low - low sensitivity
More severe effects with AR1254, but no behavioral effects observed with either treatment.	

Meerts et al. 2004	2004	626549		no	N/A
Meerts, IATM, Assink, Y, Cenijn, PH, et al.	2002	626551		yes	No neurological outcome data
Gilbert et al. 2000	2000	626689		no	N/A
Powers et al. 2006	2006	626887		no	N/A
Nguon et al. 2005	2005	629930		no	N/A
Roegge et al. 2004	2004	629932		no	N/A
Widholm et al. 2004	2004	629934		no	N/A

open field testing brain weight passive avoidance dopamine and serotonin metabolites auditory thresholds (brain stem auditory evoked potentials BAEPs)	Activity level/motor function Brain-histological, structural, morphological Emotional state Neurotransmitter levels Sensory function	Aroclor 1254
spatial learning (Morris water maze) electrophysiology	Cognitive-behavioral tests Neurophysiology	Aroclor 1254
auditory assessment using distortion product otoacoustic emissions to assess ototoxicity and cochlear function, auditory brainstem responses to measure central nervous system auditory pathways	Sensory function	Fox River PCB mixture
righting response, negative geotaxis, startle response, rotarod cerebellar structure and protein expression (glial protein GFAP, neuronal protein L1-200, L1-80, and synaptophysin)	Activity level/motor function Brain-histological, structural, morphological	Aroclor 1254
cerebellar-dependent motor function, behavior brain weight:body weight ratio	Activity level/motor function Brain-histological, structural, morphological	Aroclor 1254
series of spatial alternation tasks (cued spatial alternation) CA, noncued spatial alternation (NCA), and delayed spatial alternation (DSA) using standard 2-lever operant testing chambers	Cognitive-behavioral tests	Aroclor 1254

Mixture		Rat	Wistar	Oral-gavage
Mixture		Rat	Long-Evans	Oral-gavage
Mixture		Rat	Long-Evans	Oral-cookie
Mixture		Rat	Sprague Dawley	Oral-gavage
Mixture		Rat	Long-Evans	Oral-cookie
Mixture		Rat	Long-Evans	Oral-cookie

Secondary				10
Secondary				6
Secondary				-28
Secondary				11
Secondary				-28
Secondary				-28



16			2	25
43			2	6
43			2	1
43			2	10
38			2	6
38			2	6

25				
6				
6				
10				
6				
6				


may be useful for susceptibility section (amphetamine)	
Assessed motor behavior using rotating rod, vertical rope climbing, and parallel bar tests. Also evaluated coexposures with MeHg. Dosing performed using spiked cookies. Assessed both male and female offspring	
also evaluated coexposures with MeHg. Dosing performed using spiked cookies. One male and one female form each litter tested (PND 110).	

Fischer, C, Fredriksson, A, Eriksson, P	2008	629956		yes	Evaluated only PCB mixtures with < 4 congeners
Sitarek, K, Gralewicz, S	2009	629957		yes	No neurological outcome data
Desaulniers et al. 2003	2003	629963		yes	Evaluated only PCB mixtures with < 4 congeners
Chu et al. 2008	2008	652364		no	N/A
Berger et al. 2001	2001	656205		no	N/A
Carpenter et al. 2002	2002	656463		yes	Evaluated only PCB mixtures with < 4 congeners
Sable et al. 2006	2006	656578		no	N/A
Sable et al. 2009	2009	656579		no	N/A
Storm et al. 1981	1981	657868	2199838	no	N/A
Sable et al.	2011	708929		yes	No neurological outcome data
Pelletier et al. 2009	2009	711505		yes	No neurological outcome data

locomotor activity: variable effects at 2 and 4 months old in PCB 153-alone treatment group		PCB 153
brain weight		Mixture: PCBs 77, 126, 169
brain weight	Brain-histological, structural, morphological	Aroclor 1254
stable state behavior, fixed interval presses, response bursts, reinforcements delivered, extinction presses, transition training, transition presses	Cognitive-behavioral tests	Aroclor 1248
Long term potentiation in hippocampus brain slices from CA1 and CA3 after acute and chronic exposure		PCB 153
differential reinforcement of high rate (DRH) operant task, DRL responses	Cognitive-behavioral tests	Fox River PCB mixture
brain body weight ratio operant task of timing and inhibitory control using differential reinforcement low rate operant tasks	Brain-histological, structural, morphological Cognitive-behavioral tests	Fox River PCB mixture
open field testing conditioned avoidance response training	Activity level/motor function Emotional state	Aroclor 1254
		Fox River PCB mixture

Congener		mice	NMRI	oral-gavage
Congener		rat	Sprague Dawley	oral-gavage
Mixture				
Mixture		Rat	Sprague Dawley	Oral-diet
Congener		Rat	Wistar OR Sprague Dawley	Oral-diet
Mixture		rat	Long-Evans	Oral-cookie
Mixture		rat	Long-Evans	Oral-cookie
Mixture		Mouse	ICR	Oral-diet
Mixture		Rat	Long-Evans	Oral-cookie

				23
Primary		30		
Secondary				7
Secondary				-28
Secondary				-28
Secondary				-3
Secondary				-28



42				
43				
43			2	1
43			2	1
43	44	49	3	11
43			2	3

6				
3				
82				
6				

needs conversion (1 mL of 0.5 ug/g AR1248 added to 30 g food portion)

also MeHG (methyl mercury) and PCB co-exposures	
also MeHG (methyl mercury) and PCB co-exposures	
dose administered needs some extrapolation; also feeding occurred following a 23 hour fast- animal stress concerns?	Medium
2 rat strains used. Dosing administered on cookies. Compares effects to Lead Acetate	
Dosing performed using spiked cookies. at PND 235 tested on differential reinforcement of high rate operant task (DRH), testing on differential reinforcement of low rate operant task (DRL). Extinction measured inter response times. Researched observed deficits in inhibitory control	Related to 2919792
also evaluated coexposures with MeHg. Dosing performed using spiked cookies.	Related to 2919792

Yang et al. 2009	2009	758056		no	N/A
Tewari, N; Kalkunte, S; Murray, DW; Sharma, S	2009	758057		no	N/A
Dickerson et al. 2011	2011	759764		yes	No neurological outcome data
Jolous-Jamshidi et al. 2010	2010	759768		yes	Evaluated only PCB mixtures with < 4 congeners
Haave, M; Bernhard, A; Jellestad, FK; Heegaard, E; Brattelid, T; Lundebye, AK	2011	759809		yes	Evaluated only PCB mixtures with < 4 congeners
Johansen, EB, Knoff, M, Fonnum, F, et al.	2011	759813		yes	Evaluated only PCB mixtures with < 4 congeners

Morris water maze (escape latency, animal reach criterion)	Cognitive-behavioral tests	Aroclor 1254
righting reflex	Activity level/motor function	Aroclor 1254
immunohistochemistry ERA, kisspeptin, and coexpression of Foxin GnRH neurons, 48 gene expression array, female anteroventral periventricular nucleus fiber density. Primary effects on female hypothalamus		Aroclor 1221
		Mixture: PCBs 47, 77
neurobehavioral testing: grasping reflex, righting reflex, climb/hang test, auditory startle, visual placing, cliff drop aversion, forelimb strength, open field for spontaneous behavior, anxiety and reactivity, startle reflex (prepulse inhibition) brain macro-anatomy (MRI) serum thyroid hormone levels (free T3, free T4, TSH)		PCB 153
operant conditioning: variable effects of PCB 153 and PCB 180; Ø effect of PCB 52		PCB 52 PCB 153 PCB 180

Mixture		Rat	Long-Evans	Oral-cookie
Mixture		Mouse	C57BL/6 wild type and IL-10 <sup>-/-</sup> counterpart s	Injection-ip
Mixture		Rat	Sprague Dawley	SC injection
Congener		Rat	Sprague Dawley	oral-diet
Congener		mouse	BALB/c	oral-diet
Congener		rat	Wistar Kyoto	oral-diet?

Secondary				-14
Secondary				4
Secondary		2		
Secondary				1
Secondary				0



43			2	1
12			2	24.5
42				
41				

6				
24.5				

Dose calculated from reported dose of 500 µg/day (0.5 mg/d ÷ 0.0204 kg)

also includes some invitro mechanistic data about RyR and PCB-95 & PCB-66 specifically. Also includes PCB congener levels in brain tissue- ADME Assessed both male and female offspring	
MOA, reproductive. Primary effect is brain sexual differentiation	
this study had six groups: Casein-based control diet (that produced no viable pups for testing), Fish control diet (that incorporated Alaskan salmon into the feed), Casein diet with low PCB, Fish diet with low PCB, Casein diet with high PCB, and Fish diet with high PCB	

He, P, Wang, A, Niu, Q, et al.	2011	759818		yes	Evaluated only PCB mixtures with < 4 congeners
Molnár et al. 2011	2011	759824		yes	Evaluated only PCB mixtures with < 4 congeners
Dickerson et al. 2011	2011	759826		yes	No neurological outcome data
Boix, J, Cauli, O, Leslie, H, et al.	2011	759830		yes	Evaluated only PCB mixtures with < 4 congeners

<p>thyroid hormones (2 months old): ↑ serum T4, Ø effect on T3 or TSH</p> <p>spatial learning and memory (MWM): ↑ latency to reach the platform (average of all trials during spatial learning phase?), ↓ time in platform quadrant during probe test (↓ ratio of platform quadrant to total quadrants)</p>		PCB 153
<p>immunohistochemistry, apoptosis and gene expression in the preoptic area-anterior hypothalamus (POA), including the anteroventral periventricular (AVPV) and medial preoptic nucleus (MPN)</p>	Brain-histological, structural, morphological	Aroclor 1221
<p>locomotor activity: Ø effect in PCB 152 animals; ↓ activity in male (not female) PCB 180 animals; ↓ activity in male and female PCB 138 animals</p> <p>Extracellular neurotransmitter levels: ↓ glutamate in any PCB exposed animals; ↑ dopamine in male and female PCB 180 animals (no effect of PCB 52 or 138)</p>		<p>PCB 52</p> <p>PCB 153</p> <p>PCB 180</p>

Congener		rat	Sprague Dawley	oral-gavage
Congener				
Mixture		Rat	Sprague Dawley	Injection-sc
Congener		rat	Wistar	oral-diet (sweet jelly bit)

Secondary				16
Secondary				7



18			2	1
43				

1				


also PBDE-47 and PCB 153 co-exposures	
MOA, reproductive Primary effect is brain sexual differentiation	

Lilienthal et al. 1997	1997	784785		yes	Evaluated only PCB mixtures with < 4 congeners
Morse et al. 1993	1993	784838		yes	No neurological outcome data
Branchi et al. 2002	2002	787645		no	N/A
Anon 1983	1983	827989		yes	Not relevant for PCB hazard identification
Boix et al. 2010	2010	871983		yes	Evaluated only PCB mixtures with < 4 congeners
Piedrafita et al. 2008	2008	891025		yes	Evaluated only PCB mixtures with < 4 congeners
Piedrafita et al. 2008	2008	891063		yes	Evaluated only PCB mixtures with < 4 congeners
Iatropoulos et al. 1977	1977	1065030		yes	Abstract only

drug discrimination, thyroid hormone levels		PCB 77
plasma thyroid hormone levels and type II thyroxine 5'-deiodinase (5'D-II) activity in the brain		PCB 77 PCB 169
modified Fox battery: righting reflex, forelimb stick grasp reflex, forelimb placing reflexes, vertical screen test, screen climbing test, pole grasping open field test, thigmotaxis ultrasonic vocalizations, homing test	Activity level/motor function Emotional state Social behavior	Aroclor 1254
cognitive function, motor coordination in 3-4 month old rats, Y maze condition discrimination task, glutamate nitric oxide cGMP pathway (NMDA increased in extracellular cGMP in cerebellum)		PCB 52 PCB 138 PCB 180
		PCB 126 PCB 153
Y-maze (acquisition) and analysis of the glutamate-NO-cGMP pathway		PCB 126 PCB 153

Congener		Rat	Wistar	Injection - subcutaneous
		Rat	Wistar	Oral-gavage
Mixture		Mouse	CD-1	Oral-gavage
Congener		Rat	Wistar	Oral-diet
Congener		Rat	Wistar	Oral-diet
Congener		Rat	Wistar	Oral-diet

Secondary				7
Secondary		Expt I: 1 Expt II: 19		
Secondary				6
Secondary				7
Secondary				7
Secondary				7



18				
43			2	6
43				
43				
43				

6				


same study evaluated BDE-99	
only mild behavioral changes reported; focus of report on skin and liver changes	
Delivered PCBs in a sweet jelly bit. Learning/motor coordination/microdialysis experiments performed at 3 months males and 4 months females	

Lee, DW; Notter, SA; Thiruchelvam, M; Dever, DP; Fitzpatrick, R; Kostyniak, PJ; Cory- Slechta, DA; Opanashuk, LA	2012	1293792		no	N/A
Poon et al. 2011	2011	1293944		no	N/A
Lilienthal et al. 2011	2011	1294233		yes	Evaluated only PCB mixtures with < 4 congeners
Nakagami et al. 2011	2011	1294586		yes	Exposure design deficiencies
Vitalone et al. 2010	2010	1294892		yes	Evaluated only PCB mixtures with < 4 congeners
Gralewicz et al. 2009	2009	1295318		yes	Evaluated only PCB mixtures with < 4 congeners

locomotor activity striatal dopamine levels	Activity level/motor function Neurotransmitter levels	Aroclor 1254
DPOAE amplitudes	Sensory function	Fox River PCB mixture
		PCB 52 PCB 180
Maternal PCB concentration correlated negatively with infant social and other (grooming, locomotor, etc) behaviors		
assessed spatial learning and memory using the Morris water maze, anxiety and locomotor activity using the elevated plus maze and open field test, and passive avoidance		PCB 126
spontaneous locomotor activity (open field test), spatial short term memory (radial maze test), long term memory (passive avoidance test), sensitivity to pain and vulnerability to stress (hot plate test), efficiency of sensorimotor gating (startle response test) and sensorimotor coordination (rotarod test). Effects from PCBs on locomotor activity and rotarod performance		PCB 153

Mixture		Mouse	C57BL/6	Oral-diet
Mixture		Rat	Long-Evans	Oral-cookie
Congener		Rat	Sprague Dawley	oral-gavage
		Monkey	Macca fascicularis	natural exposure through diet and environment
Congener		Rat	Wistar	oral-diet
Congener		Rat	Wistar	Oral-gavage

Primary		28		
Secondary				-28
Secondary		PCB 52: 10 PCB 180: 4		
Secondary				7
Secondary				6



				6
43			2	3
43				
43				

25				
6				


the test substance was incorporated into a vanilla wafer cookie; ADME data includes PCB congener profiles in brain tissues; other MOA data included oxidative stress-related protein expression in the striatum and cerebellum and iron regulatory protein expression in the brain	
natural exposure to PCBs -stratified mother infant pairs into high and low PCB groups	
also examined coexposure to MeHg	

He, P; Wang, AG; Xia, T; Gao, P; Niu, Q; Guo, LJ; Chen, XM	2009	1295505		yes	Evaluated only PCB mixtures with < 4 congeners
Zimmer et al. 2009	2009	1295857		yes	Evaluated only PCB mixtures with < 4 congeners
Eriksson, P; Fischer, C; Fredriksson, A	2006	1297893		yes	Evaluated only PCB mixtures with < 4 congeners
Colciago et al. 2006	2006	1297940		yes	No neurological outcome data
Lilienthal et al. 2006	2006	1298501		no	N/A
Simmons et al. 2005	2005	1299587		yes	Evaluated only PCB mixtures with < 4 congeners
Shiota 1976	1976	1300832		no	N/A
Carter and Cameron 1977	1977	1301047	2156505	yes	Evaluated only PCB mixtures with < 4 congeners
Narbonne et al. 1978	1978	1301412		yes	No neurological outcome data
Yang et al. 2003	2003	1303281		yes	No neurological outcome data
Seegal et al. 1985	1985	1303483		no	N/A

learning and memory capacities (Morris water maze test) hippocampal ultrastructure		PCB 153
		PCB 126 PCB 153
spotaneous behavior (4 and 6 months old) habituation capability (4 and 6 months old)		PCB 52
expression of testosterone activating enzymes in the hypothalamus		Aroclor 1254
brain weight sweet preference	Brain-histological, structural, morphological Sexual behavior	Aroclor 1254
assessed the effect of PCB 77 on maternal behavior, including nest-building, nursing, and grooming of pups		PCB 77
open field test water T-maze test	Activity level/motor function Cognitive-behavioral tests Emotional state	Kanechlor 500
organ weights, brain histology, neuromuscular coordination (rotarod)		PCB 153
ATPase activity in brains and livers measure--relevant to MOA		
Urinary homovanillic acid concentrations	Neurotransmitter levels	Aroclor 1016 Aroclor 1260

Congener		rat	Sprague-Dawley	oral-gavage
Congener		goats	Norwegian breed	oral-diet?
Congener		mouse	NMRI (Naval Medical Research Institute)	oral-gavage
Mixture		Rat	Sprague Dawley	Oral-gavage
Mixture		Rat	Long-Evans	Injection-sc
Congener		rat	Long-Evans	subcutaneous injections
Mixture		rat	Sprague-Dawley-JCL	Oral-gavage
Congener		Mouse	Swiss Albino	Oral-gavage
Mixture		rat	Wistar	Oral-gavage

Secondary		91		
Secondary				15
Secondary				10
Secondary		7		
Secondary				8 15
Primary		1		
Primary		1		



19			2	25
18			2	30
14 21			2	20
			2	500

25				
30				
100				
1000				


combined exposure to PCB 153 and PBDE 47 was also studied	
combined exposure to PCB 52 and PBDE 99 was also studied	
likely will be only a reproductive study- repro behavior	
provides data relevant for ADME	

Geller et al. 2000	2000	1309819		yes	Evaluated only PCB mixtures with < 4 congeners
Elnar et al. 2012	2012	1323584		no	N/A
Strużyńska and G. Dąbrowska-Bouta 2012	2012	1401064		yes	No neurological outcome data
Bavithra et al. 2012	2012	1402037		no	N/A
Curran et al. 2011	2011	1402199		no	N/A
Tian et al. 2011	2011	1402374		no	N/A
Coccini et al. 2010	2010	1403260		yes	No neurological outcome data
Koller and Zinkl 1973	1973	1404476		no	N/A
Aulerich and R. K. Iwamoto 1973	1973	1404635		yes	No neurological outcome data

		PCB 126
forelimb grip strength, open field, water escape pole climbing, tail suspension, vestibular function, locomotor coordination Morris water maze elevated plus maze, light dark box maternal behavior	Activity level/motor function Cognitive-behavioral tests Emotional state Social behavior	Mixture: PCBs 28, 52, 101, 138, 153, 180
		Aroclor 1254
cerebellar histopathology	Brain-histological, structural, morphological	Aroclor 1254
novel object recognition, Morris water maze neurotransmitters	Cognitive-behavioral tests Neurotransmitter levels	Mixture: PCBs 77, 105, 118, 126, 138, 153, 169, 180
open field test, tail suspension test novel object test, Y-maze test elevated plus maze test	Activity level/motor function Cognitive-behavioral tests Emotional state	Aroclor 1254
Brain weight and histopathology	Brain-histological, structural, morphological	Aroclor 1221 Aroclor 1242 Aroclor 1254
only neurological measurement is brain weight	Brain-histological, structural, morphological	

Congener		Rat	Long-Evans	oral-diet
Mixture		Mouse	Albino	Oral-gavage
Mixture		rat	Wistar	Oral-gavage
Mixture		rat	Wistar	Injection-ip
Mixture		Mouse	C57BL/6J (B6) B6.D2-Ahrd Cyp1a2 knockout	Oral-gavage
Mixture		Mouse	ICR	Oral-gavage
Mixture				

Secondary				-35
Secondary				22
Primary		14		
Primary		30		
Secondary				10.5
Secondary				29



43				
43			2	0.000001
			2	10
			2	2
27			2	6.7
43	44	64	2	6

0.0001				
10				
2				
6.7				
18				

Dose calculated from information provided in supplemental materials (total PCB dose = ((55.275 mg/kg * 0.0204 kg)*2)/(0.0204 kg * 16.5d))

MOA info on mRNA expression of brain receptors and NT changes	
Group I was vehicle control, Group II received Aroclor 1254 by injection, Group III received Aroclor 1254 by injection and quercetin (50 mg/kg/d) by gavage, Group IV received quercetin alone	
no neurological health outcomes studied in animals, but MOA data related to gene expression pathways of muscarinic receptor subtypes	
only mention that brains were collected and weighed but do not report the data in the text or results section	
contains ADME data and data for reproductive, GI, hepatic, immune; presents other organ weights as a percentage of brain weight	

Allen et al. 1975	1975	1405015		yes	Evaluated only PCB mixtures with < 4 congeners
Yamamoto et al. 1976	1976	1405257	2196656	yes	Evaluated only PCB mixtures with < 4 congeners
Platonow, NS; Meads, EB; Liptrap, RM; Lotz, F	1976	1405279		no	N/A
Zinkl	1977	1405339		yes	No neurological outcome data
Iatropoulos et al. 1977	1977	1405484	2206585	yes	Evaluated only PCB mixtures with < 4 congeners
Oishi, S; Morita, M; Fukuda, H	1978	1405559		no	N/A
Clark, DR; Stafford, CJ (1981)	1981	1406522	2199837	yes	No neurological outcome data
Clarke et al. 1984	1984	1407716		yes	Evaluated only PCB mixtures with < 4 congeners

brain histopathology	Brain-histological, structural, morphological	
measured brain weight		PCB 105
brain histopathology	Brain-histological, structural, morphological	Aroclor 1232 Aroclor 1242 Aroclor 1254
		Aroclor 1254
brain weight and histopathological analysis right after 84 day exposure or after a 28 day recovery period		PCB 31
absolute and relative brain weight, gross pathology of brain	Brain-histological, structural, morphological	Kanechlor 500
tremoring behavior		Aroclor 1260
brain weight		PCB 77

		rat	Sprague-Dawley	Oral-diet
Congener		mouse	CF-1	intraperitoneal injection
Mixture				
Mixture				
Congener		Monkey	Macaca mulatta	oral-diet
Mixture		rat	Sprague-Dawley-derived	Oral-diet
Mixture		bat	little brown bats (Myotis lucifugus)	Oral-diet
Congener		rat	Sprague-Dawley	oral-gavage

Primary		28 days		
Primary		?		
Primary		84		
Primary		28		
Primary		40		
Primary		up to 21 (followed by recovery period in some rats up to day 42)		



				100
			2	10.2
			3	#DIV/0!

100				
10.2				


<p>This study included 4 experiments: 1) single doses of PCB 52 in male and female Long-Evans rats, 2) single dose of PCB 52 in Sprague-Dawley male rats with or without pretreatment with phenobarbital or SKF 525A, 3) 4-week dietary study comparing 100 ppm Aroclor 1248 and 100 ppm PCB 52 in male Sprague-Dawley rats, and 4) 2-week gavage study with a single dose level of PCB 52 in male rhesus monkeys</p> <p>ADME data included PCB residues in the brain</p>	
<p>brain histopathology was mentioned but not evaluated</p>	
<p>dosing occurred through contaminated mealworms</p>	
<p>ADME data includes PCB 77 concentration in the brain</p>	

Mele et al. 1986	1986	1408333	2207205	no	N/A
Gillette et al. 1987	1987	1408594	2163560	yes	Evaluated only PCB mixtures with < 4 congeners
Gillette et al. 1987	1987	1408597		yes	Evaluated only PCB mixtures with < 4 congeners
Linzey	1987	1408824		yes	No neurological outcome data
Sugawara, N; Ohba, T; Nakai, K; Kakita, A; Nakamura, T; Suzuki, K; Kameo, S; Shimada, M; Kurokawa, N; Satoh, C; Satoh, H	2008	1410853		no	N/A
Simmons and Mckee 1992	1992	1411046		yes	No neurological outcome data
Seegal, RF	1994	1411680	2183782	no	N/A

operant conditioning (fixed-interval schedule of food reinforcement, reinforcement omission procedure)	Cognitive-behavioral tests	Aroclor 1248
	Brain-histological, structural, morphological	
	Brain-histological, structural, morphological	
		Aroclor 1254
grasp reflex, righting reflex, walking, negative geotaxis, cliff avoidance, spontaneous locomotion activity, open-field test brain histopathology water maze test	Activity level/motor function Brain-histological, structural, morphological Cognitive-behavioral tests Emotional state	Aroclor 1254
neurotransmitter levels	Neurotransmitter levels	Aroclor 1016 Aroclor 1254 Aroclor 1260

Mixture		Rhesus monkey	Macaca Mulatta	Oral-diet
Mixture		Mouse	White- footed (Peromyscu s leucopus)	Oral-diet
Mixture		Mouse	C57BL/6Cr	Oral-gavage
Mixture				

Secondary				Aroclor 1248 (concurrent exposure): -487 Aroclor 1248 (20 mo post-exposure): -1156 Aroclor 1248 (concurrent exposure): -548
Secondary				5



Aroclor 1248 (concurrent exposure): (3 mo of age) Aroclor 1248 (20 mo post- exposure): -608 Aroclor 1248 (concurrent exposure): (4 mo of age)			2	0.09 0.006
42			2	6

0.09 0.006				
6				

Average study dose calculated from data provided in  
Table 1 (HERO ID #199846)

Estimated dose administered reported in HERO ID  
#199761

Average study doses calculated from data provided in  
Table 3 (HERO ID #199846)

Reported study dose of 18 mg/kg-d adjusted for  
continuous exposure

<p>additional exposure group, females fed 0.5 ppm PCBs in diet three times per week for 18 months, from unknown starting time through weaning of infants at 4 months old</p> <p>Why isn't this group included as an entry in the inventory?</p>	<p>Post-exposure group: Critically Deficient. Toxicokinetic data reported by Allen et al. 1980 (201752), Bowman et al. 1981 (199846), and Schantz et al. 1989 (199761) demonstrate that there was little-to-no difference in PCB body burdens between the control and exposed groups in either dams at the time of pregnancy and lactation or offspring at any time during the experiment for groups conceived a year or more after the end of the exposure period.</p>
<p>acute (3 day) study and does not provide any outcome results for the brain</p>	
<p>acute (3 day) study and does not provide any outcome results for the brain</p>	
<p>This study uses both wild caught and laboratory-bred white footed mice.</p>	
<p>this study also examined the neurobehavioral effects of coexposure to MeHg and Aroclor 1254</p>	<p>Emotional state: Low - high risk of bias Water maze: Low - high risk of bias</p>

Orito et al. 2007	2007	1412011		yes	Evaluated only PCB mixtures with < 4 congeners
Cromwell et al. 2007	2007	1412168		yes	Evaluated only PCB mixtures with < 4 congeners
Faqi et al. 1998	1998	1414286	2195928	yes	Evaluated only PCB mixtures with < 4 congeners
Bursian et al. 2006	2006	1414577		yes	Exposure design deficiencies
Seegal 1999	1999	1414612		yes	Evaluated only PCB mixtures with < 4 congeners
Chung, YW; Clemens, LG	1999	1414725		no	N/A
Pruitt et al. 1999	1999	1414981		no	N/A

<p>rotating rod test: Ø motor coordination</p> <p>open field test: Ø total horizontal distance moved, ↓ time spent in the center, ↓ number of rearings, ↑ total duration of grooming</p> <p>social interaction test: ↓ time spent in social interaction</p> <p>forced swim stress test: ↑ serum corticosterone level after forced swimming (Ø under non-stressful conditions)</p>		PCB 126
Litter size, maternal & pup weight, food intake data, conditioned odor preference behavior		Mixture: PCBs 47, 77
brain weight at PND 65 or 140		PCB 77 PCB 126
		PCB 153
female sexual behavior (lordosis quotient, percentages of mount leave and intromission leave)	Sexual behavior	Aroclor 1221 Aroclor 1254
histological/morphological changes in hippocampal mossy fibers	Brain-histological, structural, morphological	Aroclor 1254

Congener		rat	Sprague-Dawley	oral-unspecified (presumably gavage)
Congener		Rat	Sprague Dawley	Oral-diet
Congener		Rats	Wistar	oral-gavage
		Mink	Mink Mustela	
Congener		Rat	Sprague-Dawley	oral-diet
Mixture		rat	Long-Evans	Injection-ip
Mixture		Rat	Sprague Dawley	Oral-diet

Secondary		single dose		
Secondary		NR		
Secondary		1		
Secondary		36		
Secondary				
Secondary				0



			2	2.3
50	51	82	3	125

7				
125				



Statistics were confusing- grouped litter size into small/medium/large for some analyses. Had a hard time finding the end date for exposure? Perhaps it was from GD1 until the time of testing?	
female offspring were ovariectomized and administered estradiol followed by progesterone to bring them into sexual receptivity; behavioral tests began 4 hrs after progesterone treatment; hormone-treated females were tested for sexual behavior once per week for five weeks from day 70-105; 25 females were sacrificed after the last behavior test and tyrosine hydroxylase immunoreactivity was used to identify dopaminergic neurons in the caudal incertohypothalamic region	

Geller et al. 2001	2001	1415790		no	N/A
Ceccatelli et al.	2006	1415838		yes	No neurological outcome data
Sharlin et al. 2006	2006	1416310		yes	No neurological outcome data
Sugawara, N; Nakai, K; Nakamura, T; Ohba, T; Suzuki, K; Kameo, S; Satoh, C; Satoh, H	2006	1416422		no	N/A
Chung et al. 2001	2001	1416578		no	N/A
Herr, DW; Graff, JE; Derr-Yellin, EC; Crofton, KM; Kodavanti, PR	2001	1416693		no	N/A
Taylor, MM; Crofton, KM; Macphail, RC	2002	1417198		no	N/A
Pravettoni et al. 2005	2005	1417513		yes	No neurological outcome data

operant conditioning electroretinography for retinal physiology	Cognitive-behavioral tests Sensory function	Aroclor 1254
		Aroclor 1254
grasp reflex, righting reflex, walking, negative geotaxis, cliff avoidance, open-field test, spontaneous locomotion activity Morris water maze test	Activity level/motor function Cognitive-behavioral tests	Aroclor 1254
female sexual behavior (lordosis, pacing tests)	Sexual behavior	Aroclor 1221 Aroclor 1254
visual-evoked potentials (flash-evoked potentials), somatosensory-evoked potentials (SEP <sub>cortex</sub> and SEP <sub>cerebellum</sub> ), peripheral nerve-evoked potentials (compound nerve action potential and nerve conduction velocity-evoked potentials), low-frequency auditory function (reflex modification audiometry)	Sensory function	Aroclor 1254
schedule-controlled behavior: acquisition and steady- state performance under a series of fixed-interval reinforcement schedules	Cognitive-behavioral tests	Aroclor 1254
		Aroclor 1254

Mixture		Rat	Long-Evans	Oral-gavage
Mixture				
Mixture		Mouse	C57BL/6Cr	Oral-gavage
Mixture		Rat	Long-Evans	Injection-ip
Mixture		rat	Long-Evans	Oral-gavage
Mixture		rat	Long-Evans	Oral-gavage
		rat	Sprague-Dawley	oral-gavage

Secondary				6
Secondary				6
Secondary				23
Secondary				6
Secondary				6
Secondary		5		



43			2	1
42			2	2
29	82	89	2	1.75
43			2	1
43			2	6

6				
18				
3.5				
6				
6				

Reported study doses of 6, 18, 54 mg/kg-d were adjusted for continuous exposure
Study doses calculated based on reported doses of 2.5, 5 mg (2.5 or 5 mg/(0.204 kg * 7 d))

neurotransmitter data also collected- maybe reported in a sister paper?	
righting reflex was evaluated but no results were reported	
	Related to 1410853
Study performed a developmental exposure (postnatal exposure) but also examined effects in 60 day old females with no postnatal exposure (to separate concurrent from stored PCB effects)	
assessed at 128–140 days of age	
MOA data related to expression of the arylhydrocarbon receptor system (AhR and ARNT) in the hypothalamus of fetuses exposed in utero and ADME data related to PCB concentration in the brains of fetuses and dams	

Nakai et al. 2005	2005	1417552		no	N/A
Salama et al. 2003	2003	1418293		no	N/A
Khan and Thomas 2004	2004	1418852		no	N/A
Morse et al. 1992	1992	1443711		yes	No neurological outcome data
Schantz et al. 1997	1997	1443761		yes	Evaluated only PCB mixtures with < 4 congeners
L-E et al. 1992	1992	1486360		yes	No neurological outcome data
Hu et al. 2012	2012	1509275		yes	No neurological outcome data

brain weight neurotransmitter levels	Brain-histological, structural, morphological Neurotransmitter levels	Aroclor 1254
AVPV and SON volume	Brain-histological, structural, morphological	
serotonin (5-HT) concentrations in the brainstem and frontal cortex	Neurotransmitter levels	Aroclor 1254
- THYROXINE TYPE II 5'-DEIODINASE IN FETAL AND NEONATAL RAT WHOLE BRAIN HOMOGENATES		PCB 77 PCB 169
<p>∅ in errors in the 8-arm radial arm maze (spatial working memory task)</p> <p>↓ alternation in the high dose PCB 28, 118, and 153 animals in the T maze (delayed alternation)</p> <p>↓ thyroid hormone levels (T4) at weaning in PCB 77, 118, and 153 treated animals</p>		<p>PCB 28 PCB 77 PCB 118 PCB 126 PCB 153</p>

Mixture				
Mixture		Rat	Sprague Dawley	Oral-gavage
		Rat	Wistar	Oral-gavage
Congener		rat	Sprague- Dawley	oral-gavage

Primary		1		
Secondary		Expt I: 1 Expt II: 19		
Secondary		7		



			2	


0.33 mg/g-bw

contains PCB brain concentrations- ADME	

Cauli et al.	2013	1510273		yes	Evaluated only PCB mixtures with < 4 congeners
Lesmana, R; Shimokawa, N; Takatsuru, Y; Iwasaki, T; Koibuchi, N	2014	1510294		yes	Evaluated only PCB mixtures with < 4 congeners
Capone et al. 2004	2004	1715139		yes	Abstract only
Fischer and A. Eriksson 2006	2006	1715190		yes	Abstract only
Walker et al. 2014	2014	2149404		yes	No neurological outcome data
Selvakumar et al. 2013	2013	2149762		no	N/A
Poon et al. 2013	2013	2149921		no	N/A

<p>(1) assess the effects of developmental exposure to MeHg, PCB 153 or PCB 126 on spontaneous locomotor and vertical activity and motor coordination when the rats are 2-month old; (2) assess whether perinatal exposure to combinations of MeHg with PCB153 or PCB126 alter the effects of the individual neurotoxicants; (3) follow the progression of motor alterations when the rats are 3-, 5- and 7-month old; (4) assess if the effects are similar or different in males and females.</p>		<p>PCB 126 PCB 153</p>
<p>locomotor activity in an open field circadian locomotor activity striatal dopamine level striatal dopamine receptors (D2DR, D1DR, D5DR) mRNA and protein levels</p>		<p>OH-PCB 106</p>
		<p>Aroclor 1221</p>
<p>open field test learning and memory in the 8-arm radial maze plasma neurotransmitter levels</p>	<p>Activity level/motor function Cognitive-behavioral tests Emotional state Neurotransmitter levels</p>	<p>Aroclor 1254</p>
<p>locomotor activity (beam breaks)</p>	<p>Activity level/motor function</p>	<p>Fox River PCB mixture</p>

Congener		Rat	Wistar	Oral-diet
Congener		rat	Wistar	oral-gavage
Mixture		Rat	Sprague Dawley	Injection-sc
Mixture		rat	Wistar	Injection-ip
Mixture		Rat	Long-Evans	Oral-cookie

Secondary		35		
		6 doses over 11 days (PND3, 5, 7, 9, 11, 13)		
Secondary				16
Primary		30		
Secondary				-28



18			2	0.67
			2	2
43			2	3

0.67				
2				
6				

Reported study dose of 1 mg/kg adjusted for continuous exposure

<p>Delivered PCBs in a sweet jelly bit. Also examined coexposures of PCBs with MeHg. Assessed effects on motor activity at 2 months old and then followed progression of alterations in motor function at 3,5, and 7 month olds. Pups from 3-5 dams were combined for endpoint analysis.</p>	

Faass et al. 2013	2013	2149928		yes	No neurological outcome data
Walker et al. 2013	2013	2149949		yes	No neurological outcome data
Lilienthal et al. 2013	2013	2150085		yes	Evaluated only PCB mixtures with < 4 congeners
Bursian et al. 2013	2013	2150151		yes	Exposure design deficiencies
Selvakumar et al. 2013	2013	2150247		yes	No neurological outcome data

		Aroclor 1254
measured neuroendocrine gene expression in several brain regions as a potential underlying mechanism for observed effects of PCBs on reproductive development and physiology		Aroclor 1221
↑ oxidative stress markers in the brain ↓ tight junction protein mRNA in the brain		Aroclor 1254

Mixture		Rat	Long-Evans	Injection-sc
Mixture		Rat	Sprague Dawley	Injection-sc
Congener				
		Mink	Natural dark	
Mixture		rat	Wistar	IP injection

Secondary				10
Secondary				16
Primary		30		



18			2	10
18			2	1

10				
1				



Zhang et al. 2012	2012	2150283		yes	Evaluated only PCB mixtures with < 4 congeners
Kania-Korwel et al. 2012	2012	2150533		yes	Evaluated only PCB mixtures with < 4 congeners
Skipor et al. 2012	2012	2150877		yes	Evaluated only PCB mixtures with < 4 congeners
Pratheepa Kumari et al. 2011	2011	2151606		no	N/A
Miller et al. 2010	2010	2152705		yes	No neurological outcome data

<p><u>Single dose experiments</u></p> <p>Ø BBB permeability in mice treated with PCB 153 alone (↑ permeability in PCB-153-nanoparticles treated mice)</p> <p>Ø tight junction protein expression in brain microvessels of mice treated with PCB 153 alone (↓ expression of occludin and claudin-5 in brain microvessels of PCB 153-nanoparticles treated mice)</p> <p>↑ inflammatory response in brain capillaries (↑ mRNA levels of TNF-<math>\alpha</math>, IL-1<math>\beta</math>, and ICAM-1 but not VCAM-1) in mice treated with PCB 153 alone (all four elevated in mice treated with PCB 153-nanoparticles)</p> <p>transcapillary migration of monocytes in brain microvessels: enhanced in mice treated with PCB 153-nanoparticles and significance not reported for mice treated with PCB 153 alone</p> <p>experimental stroke model: ↑ infarct volume induced by ischemia/reperfusion in mice treated with PCB 153-nanoparticles and significance not reported for mice treated with PCB 153 alone</p> <p><u>30-day experiment</u></p> <p>Ø leukocyte attachment to cerebral vessels in mice treated with PCB 153 alone (enhanced aggregation in mice treated with PCB 153-nanoparticles)</p>		PCB 153
exposure had variable effects on thyroid and luteinizing hormone levels, and LH pulse frequency		PCB 153
brain histology	Brain-histological, structural, morphological	Aroclor 1254

Congener		mouse	C57BL/6	single dose experiments: ICA (internal carotid artery) injection 30-day experiment: oral- gavage
Congener				
Congener		Ewe		Oral-diet
Mixture		Rat	Wistar	Injection-ip
		Rat	Long-Evans	

Primary		single dose or 30 days		
Primary		16		
Primary		30		



			2	2

2				



<p>This study included a treatment group receiving PCB 153 bound to silica nanoparticles (termed PCB 153-nanoparticles), a PCB 153 alone group, a silica nanoparticles alone group, and two vehicle control groups. The 30-day experiment included ADME data: PCB levels were analyzed in adipose tissue. Other MOA data included in vitro transendothelial migration in human microvascular endothelial cells.</p>	

Perry and T. Faraone 2010	2010	2152970		yes	Evaluated only PCB mixtures with < 4 congeners
Yang and Lein 2010	2010	2153362		yes	No neurological outcome data
Bernhoft et al. 1994	1994	2153987	2192699	yes	Evaluated only PCB mixtures with < 4 congeners
Branchi et al. 2005	2005	2155131		no	N/A

<p>reflex development: Ø effect</p> <p>operant conditioning: ↑ lever presses and unnecessary tray visits (activity) in PCB 126 and 153-treated animals;</p> <p>other variable effects</p>		<p>PCB 126</p> <p>PCB 153</p>
<p>visual discrimination tests in skinner boxes</p> <p>spontaneous movement</p> <p>muscle maturation</p> <p>reflex development</p> <p>Surface righting reflex, negative geotaxis, head lifting, grip strength, Visual discrimination in skinner boxes</p>		<p>PCB 126</p>
<p>locomotion (horizontal movement, breaking of low level of infrared beams), rearing (vertical movement, breaking of high level of infrared beams)</p> <p>brain weight</p> <p>thigmotaxis (time and distance travelled immediately close to the walls, breaking of low level of infrared beams immediately close to the walls)</p>	<p>Activity level/motor function</p> <p>Brain-histological, structural, morphological</p> <p>Emotional state</p>	<p>Aroclor 1254</p>

Congener				
Congener		rat	Albino Lewis	oral-gavage
Mixture		Mouse	CD-1	Oral-gavage

Secondary		10 (every other day)		
Secondary				6



43			2	10

10				


Duplicates data from Holene et al. 1998 (202325)	
brain PCB concentrations reports-ADME	
also evaluated BDE-99	

Cummings et al. 2008	2008	2155713		yes	Evaluated only PCB mixtures with < 4 congeners
Hojo, R; Kakeyama, M; Kurokawa, Y; Aoki, Y; Yonemoto, J; Tohyama, C	2008	2156090		yes	Evaluated only PCB mixtures with < 4 congeners
Vitalone et al. 2008	2008	2156554		yes	Evaluated only PCB mixtures with < 4 congeners
Lee, CK; Kang, HS; Kim, JR; Lee, BJ; Lee, JT; Kim, JH; Kim, DH; Lee, CH; Ahn, JH; Lee, CU; Yu, SJ; Kang, SG	2007	2157496		yes	No neurological outcome data
Chu et al. 2005	2005	2157748		no	N/A
Coccini et al. 2008	2008	2158004		yes	Evaluated only PCB mixtures with < 4 congeners
Cummings et al. 2005	2005	2158727		yes	Evaluated only PCB mixtures with < 4 congeners
Curran et al. 2011	2011	2158756		yes	Abstract only
Muthuvel et al. 2006	2006	2159859		no	N/A

On PND 0, pups were either kept with own mother or cross-fostered with a dam from a different treatment group, so there are four treatment groups ((Oil-Oil, Oil-PCB, PCB-Oil, and PCB-PCB) that were exposed to control or PCB treatments gestationally and postnatally. Assessed sexual behavior, partner preference tests		PCB 77
learning behavior: response rate and reward rate in the fixed-ratio component and the differential reinforcement of low rates component		PCB 126
		PCB 126
		Aroclor 1254
brain weight	Brain-histological, structural, morphological	Aroclor 1254
behavioral interactions between the dams and their litters		PCB 77
hypothalamus weight	Brain-histological, structural, morphological	aroclor 1254

Congener		Rats	Long-Evans	subcutaneous injection
Congener		rat	Long-Evans Hooded	oral-gavage
Congener		Rat	Wistar	oral-diet
		rat	Sprague- Dawley	oral-gavage
Mixture		Rat	Sprague Dawley	Oral-cookie
Congener		Rats	Long-Evans	subcutaneous injection
Mixture				

Secondary		12		
Secondary		single dose		
Secondary		35		
Secondary		32		
Secondary				1
		12		



45			2	15

15				


Erratum published (HERO ID 2158725)	
learning behavior assessed beginning at 11 weeks of age	
Mating index was evaluated using a method that included no social behavior component.	
Main focus of the paper is an organochlorine mixtures study, AR1254 used as a positive control	
MOA only, assess the effect of antioxidant treatment on the amelioration of PCB-induced oxidative stress in the brain	

Donahue, DA; Bowen, CL; Provost, TL; Meserve, LA	2002	2160093		yes	No neurological outcome data
Hany et al. 1998	1998	2165213		yes	Abstract only
Roth-Härer et al. 2001	2001	2166319		yes	Evaluated only PCB mixtures with < 4 congeners
Kuriyama, SN; Chahoud, I	2001	2171606		yes	Full text not available
Lamb, JG; Smith-Yockman, MD; Constance, J; Poerschke, R; Franklin, MR; White, SH	2006	2171916		yes	Abstract only
Fanini et al. 1990	1990	2172957		no	N/A
Lilienthal et al. 1997	1997	2173279		yes	Full text not available
Lilienthal et al. 1999	1999	2173283		yes	Abstract only
Lilienthal, H; Altmann, L; Hany, J; Kaya, H; Roth-Härer, A	1998	2173288		yes	Abstract only
Lutz et al. 2008	2008	2174528		yes	Evaluated only PCB mixtures with < 4 congeners
Seegal et al. 1985	1985	2175561	2198848	no	N/A
Monaikul, S; Eubig, P; Floresco, S; Schantz, S	2013	2177050		yes	Abstract only
Schmoldt et al. 1977	1977	2179041		no	N/A

		Aroclor 1254
locomotor activity and exploratory behavior aggressive behavior, nonsocial behavior	Activity level/motor function Social behavior	Fenclor 54
		PCB 153
regional brain differences in norepinephrine levels	Neurotransmitter levels	Aroclor 1016 Aroclor 1260
brain weight	Brain-histological, structural, morphological	Clophen A30

Mixture				
Mixture		Mouse	NR	Oral-diet
Congener		Rat	Wistar	oral-gavage
Mixture		rat	Wistar	Oral-gavage
Mixture		Rat	Wistar	Oral-diet

Primary		21		
Secondary		37		
Primary		1		
Primary		84		



				1
			2	500
			3	2000

100				
1000				
2000				


some animals were house for 21 days in dark prior to behavioral testing- is this standard?	

Sanders 1977	1977	2179086		yes	No neurological outcome data
Allen et al.	1976	2179602		no	N/A
Itokawa et al.	1975	2180042		no	N/A
Platonow 1973	1973	2180503		yes	Exposure design deficiencies
Soeda et al. 2005	2005	2184699		yes	Evaluated only PCB mixtures with < 4 congeners
Soeda et al. 2003	2003	2184700		yes	Full text not available

		Aroclor 1254
brain weight	Brain-histological, structural, morphological	Aroclor 1242 Aroclor 1254 Aroclor 1262
brain weight and histopathology	Brain-histological, structural, morphological	Kanechlor 500
brain histopathology	Brain-histological, structural, morphological	
↑ambulation and rearing in the open field test in male and female pups, some other behavioral changes in females ↻ change in passive avoidance responses ↻ change in growth, reproductive, and developmental parameters		OH-PCB122

Mixture		mouse	white-footed ( <i>Peromyscus leucopus</i> )	oral-diet
Mixture				
Mixture				
Mixture		mink	NR	Oral-diet
Congener		mouse	DDY	

Primary		21		
Primary	365	105		
Secondary		7		



			3	0.64

3.57				


<p>Mice were divided into 2 feeding groups: ad libitum or 70% ad libitum (restricted diet). After 2 weeks on their feeding regimes, the 2 groups were each divided into 3 groups and were fed one of three levels of Aroclor 1254 for 3 weeks. The ad libitum-fed mice received diets containing 0, 25, or 100 ppm Aroclor 1254, and the restricted-fed mice received the same diets at 70% ad libitum containing 0, 36, or 143 ppm Aroclor 1254</p>	
<p>ADME data included PCB residues in the brain</p>	

Swiercz, R; Grzelinska, Z; Majcherek, W; Wiaderna, D; Lutz, P; Sitarek, K; Wasowicz, W; Gralewicz, S	2008	2185565		yes	Evaluated only PCB mixtures with < 4 congeners
Villeneuve et al. 1971	1971	2187123	2199350, 2181176	no	N/A
Carcinog Program 1978	1978	2192571		no	N/A
Lilienthal and Winneke 1992	1992	2192631		yes	Abstract only
Seo et al. 1995	1995	2192680		yes	Abstract only
Zahalka et al. 1995	1995	2192683		yes	Abstract only
Schantz and J. Seo 1995	1995	2192725		yes	Full text not available
Morse et al. 1995	1995	2192731		yes	Abstract only
Altmann et al. 1997	1997	2192774		yes	Abstract only
Stewart et al. 1999	1999	2192819		Yes	Abstract only
Lilienthal et al. 2000	2000	2192868		yes	Full text not available
Bushnell et al. 2001	2001	2192880		yes	Abstract only
Hany et al. 2000	2000	2192898		yes	Abstract only
Wimmer, J., Chung, Y., Wee, B., Clemens, L., Nunez, A.	2001	2192923		Yes	Abstract only
Bowers et al. 2003	2003	2192931		yes	Abstract only

offspring brain weight and relative brain weight brain catecholaminergic systems: adrenaline, noradrenaline, dopamine, and 3,4- dihydroxyphenylacetic acid (DOPAC) concentrations determined in the olfactory bulb, hippocampus, striatum, occipito-temporal cortex, diencephalon, mesencephalon, and cerebellum		PCB 153
brain weight	Brain-histological, structural, morphological	Aroclor 1221 Aroclor 1254
brain histopathology	Brain-histological, structural, morphological	Aroclor 1254
measures electrophysiology postnatal days 11-19 and paired-pulse potentiation of hippocampal slices; measures ortho and coplanar congeners		













<p>offspring were 90–97 days old at time of this experiment;  this study also examined the effects of coexposure to  MeHg and PCB 153 on brain catecholamine contents;  neurodevelopmental effects during the preweaning  period were tested but not reported in this publication</p>	
<p>should attempt to get full text; this is relevant to  neurotox</p>	
<p>Identified in targeted literature search (cognitive effects,  affective and social behavior)</p>	
<p>NBTS abstract only</p>	

Weinand-Haerer et al. 1997	1997	2195794		yes	Evaluated only PCB mixtures with < 4 congeners
Lucier et al. 1978	1978	2196056		yes	Evaluated only PCB mixtures with < 4 congeners
Seo, B. W., Moshtaghian, J., Moore, R. W., Peterson, R. E., Schantz, S. L.	1994	2196215		yes	Abstract only
Chou and T. Davis 1979	1979	2196245		yes	Foreign language
Vitalone et al. 2006	2006	2196759		yes	Abstract only
Honma et al. 2004	2004	2198433		yes	Full text not available
Honma et al. 2006	2006	2198435		yes	Abstract only
Crofton et al. 1997	1997	2198550		yes	Abstract only
Goldey et al. 1995	1995	2198659		yes	Abstract only
Anonymous 2006	2006	2198764		yes	Evaluated only PCB mixtures with < 4 congeners
Zahalka, E. A., Stanton, M. E., Rehnberg, G. L., Goldey, E. S., Ellis, D. H., Lau, C.	1994	2198854		yes	Abstract only
Yang and Lein 2005	2005	2199121		yes	Abstract only
Oshiro et al. 1999	1999	2199144		yes	Abstract only



Congener		rat	Wistar	subcutaneous injection
Congener		Mouse	CD-1	oral- gavage?











All fetal data deals with accumulation/excretion and developmental malformations; only dosing and exposure information related to neurodevelopment are included in this table	
Identified in targeted literature search (cognitive effects, affective and social behavior)	
Identified in targeted literature search (cognitive effects, affective and social behavior)	

Koja, T; Kishita, C; Shimizu, T; Fujisaki, T; Kitazono, M; Fukuda, T	1979	2199255		yes	Foreign language
Blanton et al. 2000	2000	2199477		yes	Abstract only
Caudle et al. 2005	2005	2199599		yes	Abstract only
Hori et al. 1986	1986	2199616		yes	No neurological outcome data
Yang et al. 2006	2006	2199768		yes	Abstract only
Seo et al. 1998	1998	2200148		yes	Full text not available
Bowers et al. 2004	2004	2200232	3785464	yes	Abstract only
Zepp R L and Kirkpatrick 1976	1976	2200318		yes	No neurological outcome data
Widholm et al. 1999	1999	2200469		Yes	Abstract only
Calandra	1976	2201050		yes	No neurological outcome data
Crofton et al. 1998	1998	2201264		yes	Abstract only
Widholm et al. 2000	2000	2201268		yes	Full text not available
Buitenhuis, C, Bergman, A, Gutleb, A, et al.	2006	2201281		yes	Abstract only
Goldey et al. 1994	1994	2201792		yes	Full text not available
Crofton et al. 2001	2001	2202483		yes	Abstract only
Matter, CF; Sager, DB; Girard, DM	1988	2203285		yes	Abstract only
Grant et al. 1972	1972	202477	2204253	no	N/A
Driver et al. 1999	1999	2204405		yes	Abstract only
Bowers et al. 2001	2001	2204420		yes	Abstract only
Miniats and N. S. Geissinger 1978	1978	2204540		yes	No neurological outcome data
Herr et al. 1996	1996	2204625		yes	Abstract only
Kreitzer and Heinz 1974	1974	2204969		yes	Non-mammalian species only
Mizunoya et al. 1974	1974	2206446		yes	Foreign language

		Aroclor 1254
		Aroclor 1242
		Aroclor 1254
		Aroclor 1260
		Aroclor 1254
brain weight plasma and brain cholinesterase activity	Brain-histological, structural, morphological Neurotransmitter levels	Aroclor 1221 Aroclor 1254
brain histopathology: no effects reported clinical signs: incoordination and coma		Aroclor 1254

Mixture				
		Rat		
Mixture		Rat	Wistar	Oral-diet
Mixture		Swine	germfree Yorkshire	Oral-diet

Primary		365		



			3	2
			2	12.5





abstract only	
mating index was evaluated using a method that did not measure social behavior	
ADME data included PCB residues in the brain including a comparison between conventional and germfree pigs	
method details in Felt et al. 1977, 202259	

Bowman, R. E.	1982	2206596		yes	Review
Reilly et al. 2015	2015	2919758		no	N/A
Meyer, AE; Miller, MM; Nelms Sprowles, JL; Levine, LR; Sable, HJ	2015	2919792		no	N/A
Poon et al. 2015	2015	2920043		no	N/A
Dridi et al. 2014	2014	2920095		yes	Exposure design deficiencies
Lilienthal et al. 2015	2015	2920120		yes	Evaluated only PCB mixtures with < 4 congeners
Naveau, E; Pinson, A; Gérard, A; Nguyen, L; Charlier, C; Thomé, JP; Zoeller, RT; Bourguignon, JP; Parent, AS	2014	2920420		no	N/A

open field elevated plus maze, fear conditioning mate preference sociability/novelty	Activity level/motor function Emotional state Sexual behavior Social behavior	Aroclor 1221
pup relative brain weight inhibitory control performance: differential reinforcement of low rates (DRL) 15 performance (ratio of reinforced:nonreinforced lever presses and reinforcers earned)	Brain-histological, structural, morphological Cognitive-behavioral tests	Fox River PCB mixture
audiogenic seizures	Sensory function	Fox River PCB mixture
Ø immediate working memory (% spontaneous alternation) in the Y-maze (PND38) Ø spatial learning (escape latency) and retention memory (escape latency) in the Morris water maze (PND120–123)		
Haloperidol-induced catalepsy, brainstem auditory evoked potentials (BAEPs), thyroid hormone levels		PCB 74 PCB 95
fetal cerebral cortex development: neuronal progenitor proliferation, cell cycle exit, differentiation rate, cell death, radial migration, and cortical laminar organization	Brain-histological, structural, morphological	Aroclor 1254

Mixture		Rat	Sprague Dawley	Injection-ip
Mixture		rat	Long-Evans	Oral-cookie
Mixture		Rat	Long-Evans	Oral-cookie
		mice	Swiss albino (CD 1)	oral-diet
Congener		Rat	Long-Evans	Oral-diet (jelly)
Mixture		rat	Wistar	Oral-cookie

Secondary				16
Secondary				-28
Secondary				-28
Secondary		36		
Secondary		19		
Secondary				6



18			2	0.3
43			2	3
43			2	1
20			2	6

0.7				
6				
6				
6				

Reported study doses of 0.5, 1 mg/kg were adjusted for continuous exposure

Identified in targeted literature search (cognitive effects, affective and social behavior)	
a stock solution of the Fox River PCB mixture (Kostyniak et al., 2005) was diluted with corn oil and pipetted onto a vanilla wafer cookie; behavioral training and testing began when the pups were 100 days old; this study also examined the effects of microinjections of the dopamine agonists bupropion, quinpirole, and SKF81297 directly into the medial prefrontal cortex (mPFC) on inhibitory control performance in adult rats that were perinatally exposed to PCBs	Cognitive function: Medium
dams were dosed with PCBs via consumption of a paste made from naturally contaminated eels rich in PCBs; metal concentrations in eel muscle was also determined	
test substance was injected into a wafer that was fed to the dams; ADME data included PCB congener analysis in the fetal brain	

Johansen et al. 2014	2014	2920488		yes	Evaluated only PCB mixtures with < 4 congeners
Nam et al.	2014	2920493		no	N/A
Lilienthal et al. 2014	2014	2920564		yes	Evaluated only PCB mixtures with < 4 congeners
Viluksela et al. 2014	2014	2926155		yes	Evaluated only PCB mixtures with < 4 congeners
Hu, X, Adamcakova-Dodd, A, Lehmler, HJ, et al.	2015	3005022		no	N/A
Lombardo, JP, Berger, DF, Hunt, A, et al.	2015	3007891		no	N/A
Folland, WR, Newsted, JL, Fitzgerald, SD, et al.	2015	3063353		no	N/A
Elnar, AA, Allouche, A, Desor, F, et al.	2016	3121413		no	N/A

ADHD like behavior (stimulus control sustained attention, number of lever presses with IRTs), movement from video recording, operant procedure. Gender and strain differences were noted by the authors.		PCB 153
open field novel object recognition elevated plus maze	Activity level Cognitive-behavioral tests Emotional state	Aroclor 1254
		PCB 52 PCB 180
↑ open field and motor activity many changes in biochemical and molecular changes many changes in organ histology and weights changes in hematology changes in hormones		PCB 180
brain weight and histopathology	Brain-histological, structural, morphological	Chicago Air Mixture
hyperactivity operant conditioning	Activity level/motor function Cognitive-behavioral tests	Aroclor 1248
brain weight and histopathology	Brain-histological, structural, morphological	Aroclor 1268
short-term spatial memory (Y-maze), long-term spatial learning and memory (MWM)	Cognitive-behavioral tests	Mixture: PCBs 28, 52, 101, 138, 153, 180

Congener		Rat	Spontaneously hypertensive (SHR/NCrl) and Wistar Kyoto	Oral-gavage
Mixture		Mouse	ICR	Oral-gavage
Congener		Rat	Sprague Dawley	oral-gavage
Congener		rat	Sprague-Dawley	oral-gavage
Mixture				
Mixture		rat	Sprague Dawley	Inhalation
Mixture				
Mixture		Mouse	swiss albino	Oral-gavage

		Unclear- 3 different dosing times between PND 8-20. Maybe single dose?		
Secondary		10 total applications for PCB 52; 4 for PCB180		
Primary		28		
Primary		30		
Secondary				22



			2	0.0003
43			2	0.00001

0.0003				
0.00001				

Study dose of 562 ng/m <sup>3</sup> converted to mg/kg-d assuming average respiration rate of 74 mL/min and an average rat weight of 0.2 kg, as in HERO ID 199578

used spontaneously hypertensive rats (SHR/NCrl) and Wistar Kyoto were the rat strains	
only brain weight (no sig difference) is reported	
also evaluated effect of injection of amyloid beta oligomers on learning and memory in PCB-treated animals	

van Esterik, JC, Verharen, HW, Hodemaekers, HM, et al.	2015	3176020		yes	Evaluated only PCB mixtures with < 4 congeners
Bandara, SB, Eubig, PA, Sadowski, RN, et al.	2016	3350985		no	N/A
Sumathi, T, Asha, D, Nagarajan, G, et al.	2016	3351130		no	N/A
Tang, W, Cheng Jin, P, Yang Yi, C, et al.	2015	3351160		no	N/A
Bell, MR, Hart, BG, Gore, AC	2016	3351276		yes	No neurological outcome data
Wahlang et al. 2016	2016	3351296		no	N/A
Bell, MR, Thompson, LM, Rodriguez, K, et al.	2016	3351306		no	N/A
Bavithra, S, Sugantha Priya, E, Selvakumar, K, et al.	2015	3351540		yes	No neurological outcome data

spontaneous locomotor activity, sucrose preference, object recognition tests: Ø effect on any neurobehavior endpoint		PCB 153
audiogenic seizures	Sensory function	Fox River PCB mixture
muscle grip strength (rotarod), locomotor activity (open field) brain histopathology spatial memory (MWM), radial arm maze	Activity level/motor function Brain-histological, structural, morphological Cognitive-behavioral tests Emotional state	aroclor 1254
righting reflex, cliff drop test response, negative geotaxis	Activity level/motor function	Aroclor 1254
<b>variable:</b> report correlations between previously reported behavior data (Bell et al., 2016 HERO ID 3351306) and changes in gene expression in different brain regions		
activity level	Activity level/motor function	Aroclor 1260
elevated plus maze and light-dark box (anxiety) sociosexual interactions ultrasonic vocalizations and affiliative behavior, sociability	Emotional state Sexual behavior Social behavior	Aroclor 1221
<b>variable</b> effects on protein expression (NMDA receptor, PKA, etc.) and mRNA expression (BDNF, NTRKB receptor, etc.) in the cerebral cortex		aroclor 1254

Congener		mice	C57BL/6JxF VB	oral-diet
Mixture		rat	Long-Evans	Oral-cookie
Mixture		rat	albino	Injection-ip
Mixture		rat	NR?	Oral-gavage
Mixture				
Mixture		rat	Sprague Dawley	Injection-ip
		rat	Wistar	IP injection

Secondary		63		
Secondary				-28
Primary		30		
Secondary				6
Secondary				16 46
Primary		30		



43			2	6
			2	2
43			2	1.5
20 50			2	0.2 0.3

6				
2				
1.5				
0.2 0.3				

Reported study dose of 1 mg/kg-d adjusted for continuous exposure

study effect of PCB and melatonin co-exposure on BDNF signaling	

Gillette et al.	2017	3982717		no	N/A
Sadowski et al.	2016	3983596		no	N/A
Monaikul et al.	2017	3983676		No	N/A

elevated plus maze and light-dark box (anxiety)	Emotional state	Aroclor 1221
neurophysiology	Neurophysiology	Aroclor 1242 Aroclor 1254 Aroclor 1260
operant behavior	Cognitive-behavioral tests	Fox River PCB mixture

Mixture		Rat	Sprague-Dawley	Injection-ip
Mixture		Rat	Long-Evans	Oral-cookie
Mixture		Rat	Long-Evans	Oral-syringe







<p>Identified in targeted literature search (cognitive effects, affective and social behavior)</p> <p>Body weights were measured during pre-puberty, adolescence, and adulthood. Listed prepubertal and adolescent weights under developmental effects. Listed adult body weights under metabolic effects. Seeking EPA review for categorization of this study.</p>	
<p>Nervous system effects are the activation/development of the auditory cortex. Mothers were exposed orally through diet, but outcomes were measured for grown offspring (brain slices).</p> <p>There were significant increases in the ratio of aCSF/SR95531 activation in slices from PCB-exposed animals compared to control animals.</p> <p>Relevant to MOA for neurological effects. The authors used GABA and NMDA receptor antagonists to explore excitatory and inhibitory neurotransmitters affected by PCBs in the auditory cortex.</p>	
<p>Identified in targeted literature search (cognitive effects, affective and social behavior)</p> <p>Cognitive function was measured by cognitive flexibility, response inhibition. There were subtle sex-specific effects of PCB exposure in adolescent rats on the reversal phase of a set-shifting task, but no effects of exposure on performance on a DRL15 task, suggesting an effect on cognitive flexibility but not response inhibition.</p>	

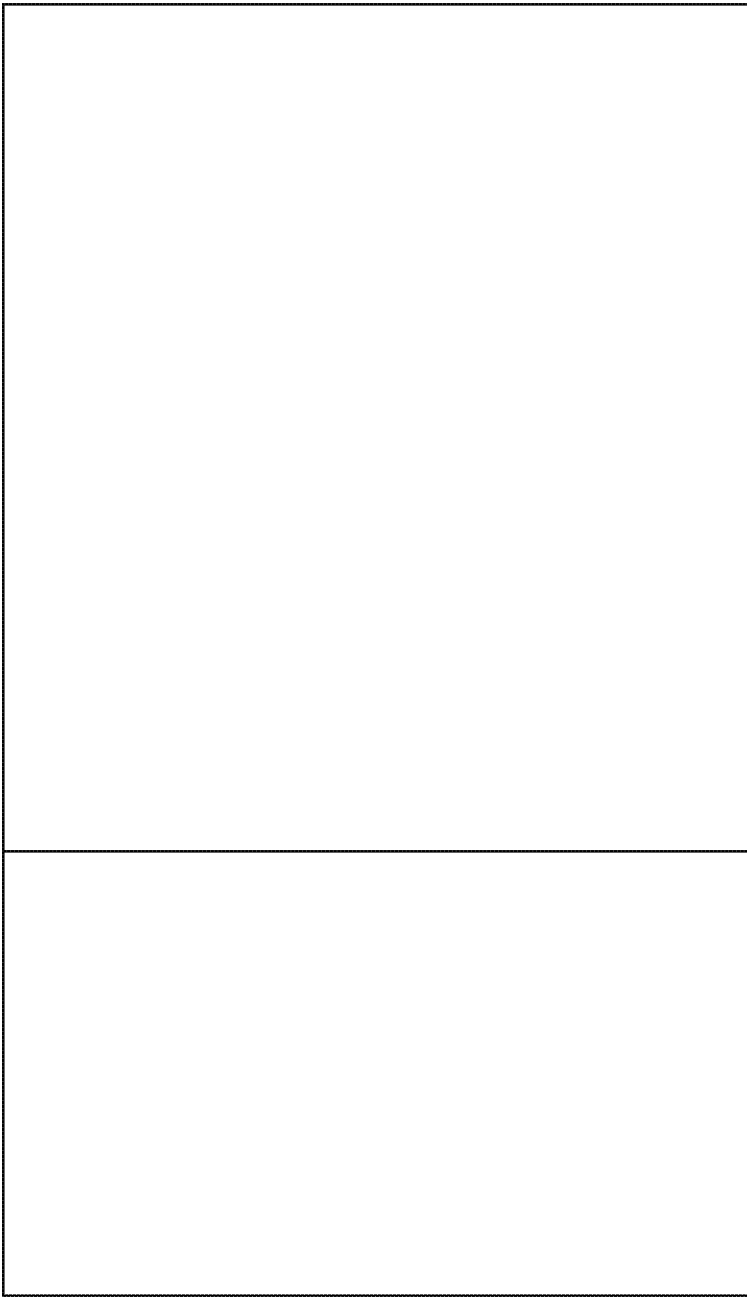
Miller et al.	2017	3984651		No	N/A
Miller et al.	2017	3985147		No	N/A

<div>activity box</div> <div>behavioral sensitization to cocaine</div>	<div>Activity level</div> <div>Emotional state</div>	<div>Fox River PCB mixture</div>
<div>operant testing</div> <div>cocaine self-administration</div>	<div>Cognitive-behavioral tests</div> <div>Emotional state</div>	<div>Fox River PCB mixture</div>

Mixture		Rat	Long-Evans	Oral-cookie
Mixture		Rat	Long-Evans	Oral-cookie





<p>Identified in targeted literature search (cognitive effects, affective and social behavior)</p> <p>Only pre-cocaine injection is data of interest.</p> <p>Administered mixture was 35% Aroclor 1242, 35% Aroclor 1248, 15% Aroclor 1254, and 15% Aroclor 1260.</p> <p>Only behavior/activity data presented. Authors state, "In the interest of brevity only significant PCB exposure and sex related effects are presented."</p> <p>Authors compare reproductive/hepatic data results to another study in the methods sections: "Physiological measures including the dam liver weight, number of embryo implantation sites in the dam, and brain:body-weight, liver:body-weight and thymus:body-weight ratios in the pups were determined, as was the percent of gestational and lactational weight-gain in the dams and postnatal body weights of the pups on PND 0, 7, 14, and 21. These measures were very similar to what has previously been reported (Sable et al., 2011)." These authors did not report on these endpoints.</p>	
<p>Identified in targeted literature search (cognitive effects, affective and social behavior)</p> <p>Nervous system effects involved changes in intravenous self-administration (IV SA) of the psychostimulant cocaine due to perinatal exposure to a PCB mixture.</p> <p>PCB exposure enhanced early cocaine drug-seeking in this preclinical model of developmental contaminant exposure (particularly in males), but no differences were seen during later cocaine SA sessions.</p>	

Bandara et al.	2017	3985418		no	N/A
Bavithra, S., Selvakumar, K., Sundareswaran, L. et al.	2017	3985422		No	N/A

neurophysiology	Neurophysiology	Fox River PCB mixture
rotarod, open field brain histopathology elevated plus maze	Activity level/motor function Brain-histological, structural, morphological Emotional state	Aroclor 1254

Mixture		Rat	Long-Evans	Oral-cookie
Mixture		Rat	Wistar	Injection-ip

Primary	NR (180-200 g males)	30		



			2	2

2	N/A	2		

Effects observed for all endpoints: rotatod, open field  
activity, elevated plus maze, brain histopathology

<p>Evaluated mixture consisting of 35% Aroclor 1242, 35% Aroclor 1248, 15% Aroclor 1254, and 15% Aroclor 1260; Measured seizure susceptibility based on electrical kindling from the amygdala.</p> <p>In the PCB exposed pups, there were significant (<math>p &lt; 0.05</math>) decreases of 8, 13 and 19% in body weight compared to controls at postnatal days 7, 14 and 21. No other gross developmental abnormalities were noted. Body weight measures taken prior to and after the kindling procedure indicate that developmentally PCB exposed animals recovered to control body weights at adulthood (&gt;PND 90).</p> <p>The neurophysiology endpoint was seizure susceptibility. This was measured by using the electrical kindling model - a model of epileptogenesis that is distinct from the audiogenic seizure model and primarily targets the limbic system as opposed to the auditory brainstem. Thus, this study explored a mechanistic model to study seizure susceptibility. However, even though these endpoints were on the mechanistic side, this study was classified as health effect, due to the direct applicability of the model.</p> <p>In the study, treated animals had attenuated focal (amygdala) excitability.</p>	
<p>Identified in targeted literature search (cognitive effects, affective and social behavior)</p>	

Parent et al.	2016	3985424		no	N/A
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hippocampal development/neurophysiology	Neurophysiology	Aroclor 1254
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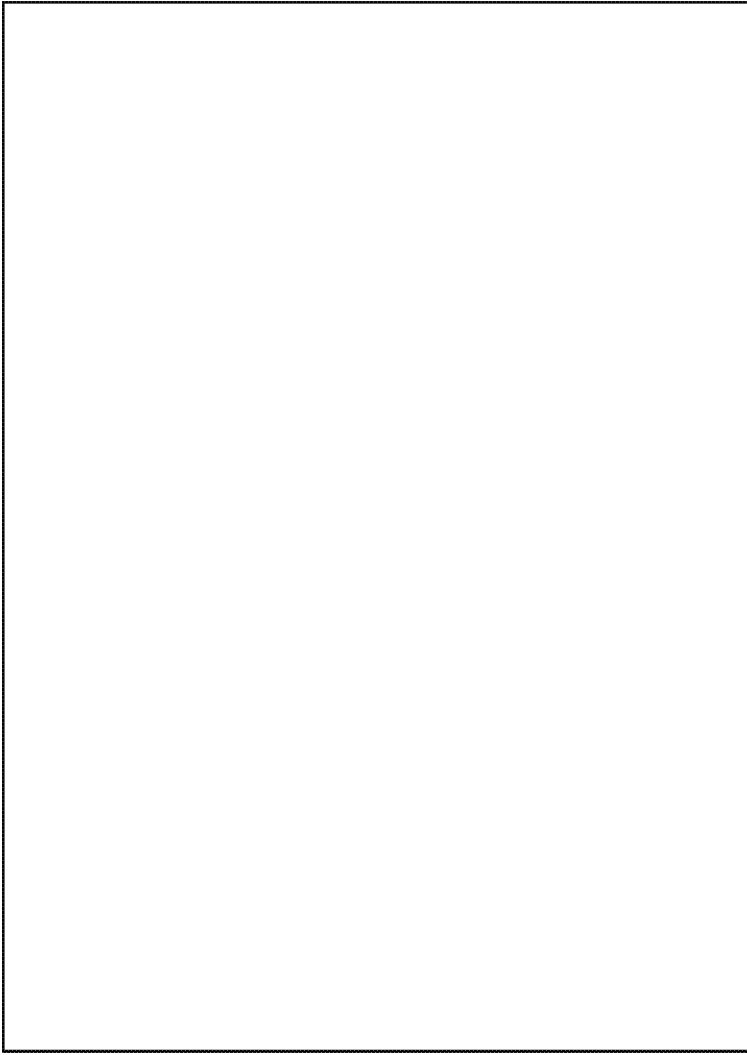
Mixture		Mouse	C57BL/6J	Oral-cookie
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<p>This is primarily a mechanistic study relevant to neurological effects (PCB disruption of the functional synaptic development of newborn hippocampal granule cells). This study also measures T4 which was listed under endocrine health effects.</p> <p>ICF included whole-cell recordings in brain slices prepared from the dentate gyrus to measure development of excitatory synapses under MOA in support of evaluating cognitive neurological effects. Although neurophysiological studies can be included as health effect data, we were not sure if this should be classified MOA because no cognitive function tests were conducted. ICF requests EPA review for including neurological effects.</p> <p>Other Relevant MOA data for neurological effects included proliferation, survival and differentiation of neurons in the dentate gyrus (fluorescence microscopy to image GFP of newly generated granule cells (delivered by stereotactic retrovirus injection) and BRDU positive cells - BRDU also delivered by stereotactic injection). Study also evaluates spine density and morphology of granule cells in newborns and older mice.</p>	
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